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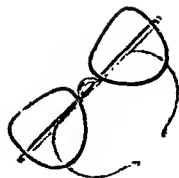
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TO HER MAJESTY  
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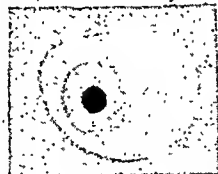
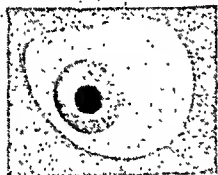
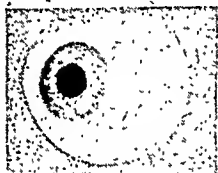
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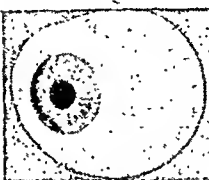
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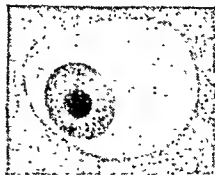
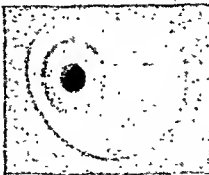
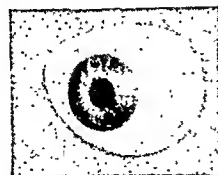


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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

JANUARY, 1948

## COMMUNICATIONS

### TWO UNUSUAL SCLERO-CORNEAL NEOPLASMS\*

BY

ARNOLD LOEWENSTEIN

GLASGOW

and

JOHN FOSTER

LEEDS

TRUE tumours of the sclera (if they in fact exist) are rare. Doubt has been cast by later investigators on most published cases.

Ginsberg, in his critical review of 1928, declared for instance that their existence must be regarded as unproven.

Fibromata are scarcely distinguishable in many cases from chronically inflamed tissue, in particular from keloidal scarring. The diagnosis of a true blastoma is also very difficult. If we except limbal melanomata and growths arising from corneal epithelium, the same is true of the cornea. Limbal swellings as a rule are neoplastic.

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\* Received for publication, July 12, 1947. From the Tennent Institute, Glasgow (Professor W. J. B. Riddell).



In general, a neoplasm composed of cells of a mature type is regarded as less malignant than a tumour with little connective tissue, and densely packed nuclei varying in size and shape, and with many mitoses.

Experience shows that the clinical course is not always correctly prophesied by the findings of biopsy. Modern cancer research has provided new facts whose clinical bearing cannot be disregarded, although divergent conclusions have been based upon them.

Cancer is a biological problem, and a purely histological investigation may be regarded as inadequate in the days to come. It is possible we have overlooked a rare opportunity in the two following cases :-

### Case I

Geoffrey H., aged 15 years—A tumour resembling a phlycten was observed on the right limbus at 11 o'clock. It increased rapidly in size over two weeks.

The growth (Fig. 1a and 1b) was yellowish, painless, hard, and restricted to the quadrant shown. The overlying conjunctiva contained dilated vessels, and was freely movable.

The vision and the eye otherwise was absolutely normal. General examination, the Wassermann and Mantoux reactions, were negative.

As the swelling doubled in size in five weeks it was removed locally and sectioned. Biopsy, July 4, 1946—The tumour 3.5 mm. in diameter was fixed in formalin and embedded in paraffin. The tumour mass of tissue is partly covered by normal epithelium, the basal line of which is infiltrated with polymorphs, lymphocytes,



FIG. 1a.  
Primary tumour.



FIG. 1b.

Primary tumour — looking down.

and many plasma cells. The major part of the tissue consists of spindle cells whose fibres cross each other and enclose a considerable number of blood vessels (Fig. 2).

The nuclei being oblong are distributed unevenly. The densest area is central, the nuclei being more sparse in the periphery. The nuclei show very few mitoses, but are variable in size and shape. There is no pigment. Certain clear spots may correspond to myxomatous and others to fatty changes. At the edge of the sections fatty tissue is actually present. Leucocytes are seen around vessels in places in considerable numbers.

We concluded from this that the tumour was a spindle sarcoma of low or moderate malignancy, though the unequal density of the tissue was rather striking.

After local excision the remaining tumour tissue continued to increase in size, contrary to the prognosis given above, and the eye was therefore excised ten weeks after the original biopsy, and fixed in formol-saline.

### The Excised Eye

The eye was sectioned equatorially and the ciliary surface of the tumour area examined by the slit-lamp (Fig. 3).

The entire retinal periphery within 6mm. of the ora serrata displayed a continuous wavy bluish white appearance. No nodules were visible. This colour change was most marked at the ora serrata underlying the tumour area, where the crests of the arcades are intensely whitish and convoluted, and can be traced over the surface of the ciliary body as far as the ciliary processes.

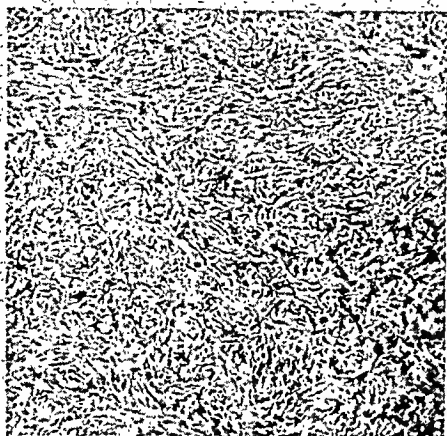


FIG. 2.

Biopsy specimen.  
Haem. Eos. appr. 150X.

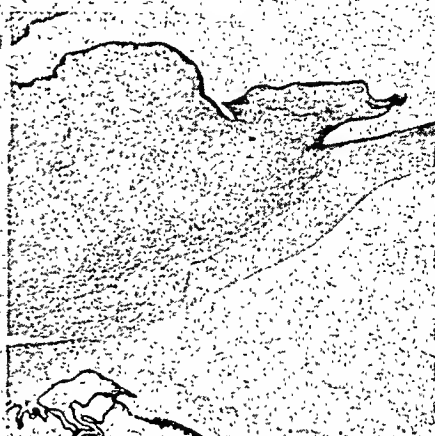


FIG. 4.

Infiltrative growth into cornea and  
sclera. H.E. 30X appr.

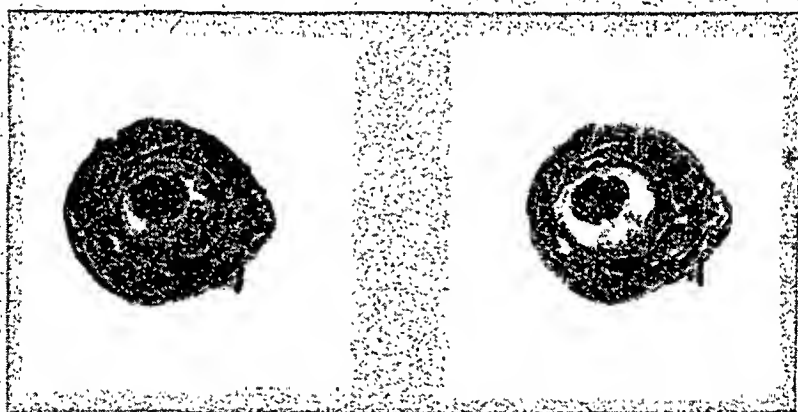


FIG. 3a.

Stereophoto — excised bulbus. Natural size.

There is little doubt that this is a continuation of the whitish layer on the peripheral retina.

Among the large portion of conjunctiva deliberately excised with the eye, can be seen a normal palpebral lacrymal gland with one duct. The vessels are congested, and there is diffuse plasmocellular infiltration.

This swollen infiltrated conjunctiva has grown over the peripheral cornea, and overlaps the un-infiltrated part of the cornea (Fig. 4).

There is no definite boundary between the inflamed tissue, and the tumour infiltrating the outer third of the cornea and sclera.



FIG. 3.



The tumour infiltration extends about 1.4 mm. from the limbus into the cornea, and remains localised to the outer lamellae. The limit of the tumour on the sclera is ill defined. It is impossible to define where the new growth in the sclera ends, and inflammatory tissue reaction starts.

The nature of the tumour coincides with the biopsy specimen, though the crisscross pattern of the spindle cells is less regular, and there are no more lymphocytes round the vessels. Pyknosis is frequent.

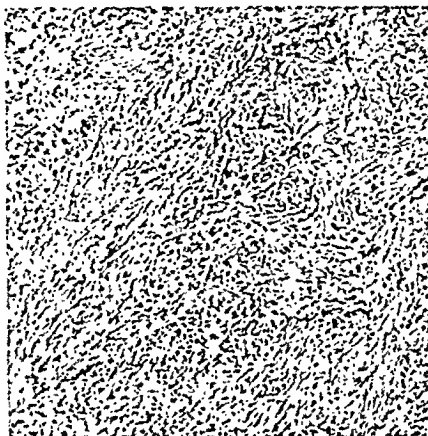


FIG. 5.

Medium power (appr. 150X) from Fig. 4X.

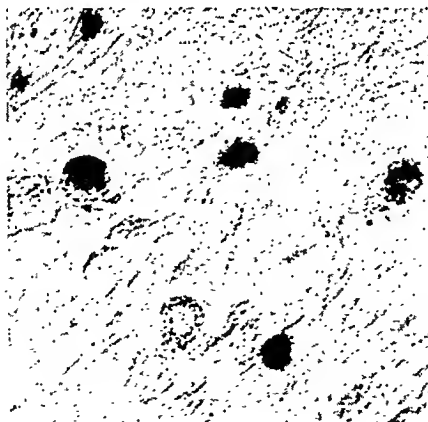


FIG. 6a.

Thionin staining at iris root. 1000X approx. Mast cells and free mast cell granules.

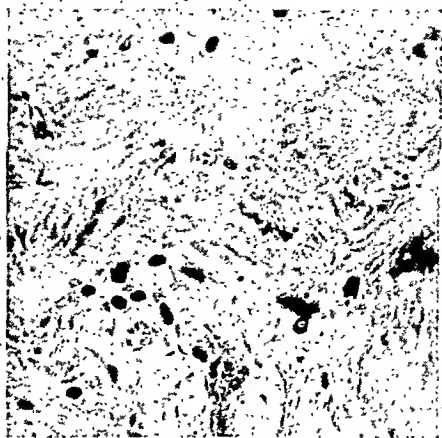


FIG. 6b.

Giemsa staining — Mast cell granules and mast cells in the outskirts of the tumour. (300 X approx.)

The fibres of the spindle cells are a greyish pink, and the intact scleral fibres with which they interlace eosin red. The photomicro does not show this colour contrast vividly in the specimen. Here and there are syncytial aggregations of ten and more nuclei, strongly suggestive of giant cells. They are located around small vessels at the edge of the growth.

Few pigment granules are seen in the trabeculae of Schlemm's canal. There is a slight eversion of the pigment epithelium, and no inflammation of the iris. The retina is, especially in its anterior part, covered by an attenuated, much convoluted layer, containing fibrils, red blood corpuscles, and fine pigment granules. It corresponds with the curled threads (Fig. 3), and is unconnected with clearly seen glassy zonula fibres.

There are an unusual number of mast cells in the iris and ciliary body, and underlying the tumour area, less frequent in the choroid. Their granules are metachromatic, and well marked with Giemsa, Leishmann, methylene-blue, but are also recognisable with Van Gieson, haematoxylin-eosin, Mallory and Masson. In contrast to the usual lobate or kidney-shaped nucleus the nuclei are here round or oval, and the cell diameter 10-14  $\mu$ . against the usual average of 8-10  $\mu$ . (Whitby & Britton, 1946).

Typical fibroblasts are visible in the growth packed with small metachroic granules.

#### Discussion (Case I)

The growth consisted of mature cells. The concentration of the nuclei was unusually variable, being diffuse in the periphery and concentrated in the centre.

The tumour infiltrates the sclera, and has no clear line of demarcation, so that even at the centre of the growth area the tumour cells are seen in the interstices of normal scleral fibres, an unusual appearance in typical malignant new growths of this area. The nuclei at the periphery of the growth assume groupings, suggesting giant cells in many places.

Masses of mast cells spread into the uvea from the tumour area.

If we add to these findings, the clinical facts that the growth was hard in consistency, painless, and rapid growing, it is not easy to classify it as a common mesodermal malignant blastoma, and casts doubt on our original diagnosis, which led to excision of a functioning eye.

It is true that the clinical appearance primarily led to this decision, but even after careful histological investigation it is difficult to "type" this growth with certainty.

Obviously it is not an infectious granuloma, nor a keloidal formation; certainly it is not a scleritis.

Our impression is of a tissue reaction to an agent, which unlike most pathogenic organisms does not produce cellular destruction but cellular division (Borrel).

Rous, in 1910, was the first to describe a tumour which was a transmissible and filterable sarcoma of chickens, followed by Fujinami and Unamoto in 1911, with their myxosarcoma. No tumours of this type have been described as yet in man.

Assumption of a virus aetiology would explain why the mode of



FIG. 7a.

Rous's sarcoma. H.E. 60X. Strands of tumour tissue growing between healthy muscle tissue.





FIG. 7b.

Fujinami's myxosarcoma. H.E. 60×

growth in our case differed from the picture we are used to find in a true blastoma of this region.

On studying the slides of two virus tumours, a Rous sarcoma and a Fujinami tumour, by the kindness of Dr. Peacock, I (A.L.) was amazed by the mode of infiltration of the new growth which splits normal muscular tissue by many tumour strands. We have found no mast cells in Giemsa stained slides—but have no information about the occurrence and behaviour of this cell form in birds.

Proof of the assumption of a virus aetiology of this new growth is a difficult matter, as a routine microscopic investigations will not at present render a virus visible unless it forms inclusion bodies. Future investigation with the electron microscope promises to show the filter passing virus particles directly.

Injection of tumour material into the anterior chamber of an animal was considered too late to apply it, and the best animal species for this purpose has yet to be established.

Virus tumours grow best in traumatized tissue especially young fibroblastic tissue according to Oberling.

No precedent trauma was observed in this case. It was pointed out, however, by Dr. Peacock (a pioneer in experimental cancer research) that a small skin dose of X-rays (600 r) might produce a local fibroblastic reaction from the virus if it was still in the circulation. As the boy had been irradiated post-operatively, we enquired but were assured by the Radiologist that no reaction of this type had been detected in or around the orbit from the first small doses used to estimate the amount of irradiation that could be safely given.

This negative finding will not, however, exclude a virus as cause, as by this time the virus might have left the circulation if in fact it had ever entered it.

The assumption of a virus aetiology for this limbal tumour, therefore, remains guesswork only.

### Case II.

Annie S., aged 65 years.—Little history could be obtained in this case. The patient stated that the left eye had always had good sight with glasses (+3.0), and that the right had been blind about fifteen years, while during the last five a growth had appeared on the eye. She denied any form of ocular injury.

On examination the lower two-thirds of the right cornea displayed a whitish cauliflower-like growth of firm consistency, elevated about 2mm. above the surface at its highest point. All investigations including the Wassermann and Mantoux reactions were negative.

The condition was obviously neoplastic, and the eye blind. Excision was performed on January 9, 1947, and the eye preserved in formol-saline.

*Histology.* The lower two-thirds of the cornea are covered by a fungus-like growth about 1.25 mm. thick (Fig. 8). An irregular epithelium two to five rows in thickness invades the growth to a



FIG. 8.

Corneal fibroma—with myxomatous and calcareous degeneration. The tumour rises from the tissue of a pannus degeneration. H.E. 30× appr.

depth of 3-500  $\mu$  thus dividing it into segments (Fig. 9). The epithelial covering is complete except for a central area of about 0.3 mm.

The cornea underlying the growth has a more or less well preserved Bowman's membrane, but no epithelial covering. The tumour itself is composed of fibrous strands of varying diameter, some containing metachromic granules. The external fibres are



FIG. 9.

Corneal fibroma. H.E. 120 $\times$  appr. Epithelial outgrowth divides the tumour in its outer rim. The deeper layers of the tumour are vascularized.

parallel, with a few interstitial nuclei. The deeper fibres are arranged in a crisscross manner, and are more vascular. Small areas without nuclei or fibres suggest myxomatous degeneration. An irregular line of calcareous tissue runs obliquely through the growth.

The tumour free area of the cornea is covered by a vascular degenerative pannus, which pierces Bowman's membrane here and there.

The corneal parenchyma is normal, except for some deep peripheral vessels.

*Iris.* There are broad root synechiae of the extremely atrophic iris, and extensive supra-intra- and pre-choroidal and pre-retinal haemorrhage.

*Retina.* The retina itself is degenerate with intra-retinal hyaline patches, which here and there penetrate the limiting membrane, and spread in a pre-retinal plane. This pre-retinal tissue contains many thin-walled vessels with a wide lumen. Giemsa staining shows many large mast-cells in the pannus, especially at the edge near the tumour. Fibroblasts within the tumour are full of metachromatic granules.

### Discussion (Case II)

Such tumours of the cornea have been described by several authors. Ginsberg (1905) referring to a corneal tumour in a nine years old child, covering the whole and destroying a considerable part of the cornea, expressed his belief that these corneal tumours are inflammatory pseudo-tumours, although they have been described as fibromata, myxofibromata, or myxomata.

Ginsberg found many mast cells and mast cell granules within the outskirts of the tumour tissue. His mast cells were as a rule unusually large (like those described in our case).

The tumour of Case II is a relatively acellular, slow growing fibroma, with a sign of regressive change in the shape of calcareous and myxomatous degeneration.

The numerous mast cells in both pannus and the tumour outskirts, and the mast cell granules filling the fibroblasts of the tumour, are reminiscent of a chronic inflammation. The growth has originated in the pannus. An unusual stimulus is supposed to have caused this type of pannus newgrowth. The stimulus might have been of mechanical, chemical, or biological nature.

If a mechanical stimulus is present, *e.g.*, by exposure to atmospheric influences, tyloma-like corneal thickening is observed frequently in such cases, *e.g.*, Loewenstein has described cystic growth of corneal epithelium after a chemical stimulus with local burning with chloroform during general anaesthesia. Ichikawa (1913) has described a typical progressive Mooren's ulcer exactly at the place where seven years before the cornea was burned by chloroform.

Nothing in the history suggests that either of the first two possibilities played any part, though one cannot exclude them entirely.

On the other hand, a biological stimulus is a possibility.

In 1931 Shope described fibromata in wild rabbits due to a transmissible filterable virus, and in 1932 a warty like growth which when transferred to domestic rabbits might undergo malignant metaplasia.

Oberling quotes a most interesting experiment performed by Green, Goodlow, Evans, Peyton, and Tifru, who transplanted a wart from the eyelid of a seventy-one year old man into the anterior chamber of three monkeys. In each case epithelial tumours developed in the anterior chamber of the monkey, and in the conjunctiva at the site where the needle penetrated.

Laryngeal papilloma, condyloma, and the common wart in man, are known to be of virus origin. We suggest, therefore, as a possibility that this conversion of pannus into tumour tissue may be due to a virus, and might be transmissible to animals. Unfortunately the idea of such an experiment came too late.

### Summary

A description is given of two unusual pathological cases:—

(a) A hard painless limbal growth of rapid growth infiltrating both cornea and sclera and with dilated vessels in the overlying conjunctiva. This was removed locally. Histologically this proved

to be a spindle cell sarcoma of a mature type, unequal cell distribution, markedly vascularised with giant cell formations in the vessel walls. A considerable number of large mast cells with a big round nucleus were present. Metachroic granules fill the plasma of certain fibroblasts and are also found free in the tissues.

As the clinical progress was more rapid than the histology would suggest, the eye was excised. A milky film was found at slit-lamp investigation covering the retinal periphery, and continued forward over the ciliary processes. There were no signs of uveitis.

It is possible that the tumour may belong to the group of neoplasms much studied in the last three decades by Rous (1910), Fujinami and Unamoto (1911), Shope (1932), and many other authors.

These authors have described transmissible tumour caused by a filterable virus in birds and wild rabbits. Angiosarcomata, myxosarcoma, and endotheliomata with a virus aetiology have been found in birds as well. Virus-caused tumours are known to exist in man, e.g., the common wart, condylomata, and laryngeal papilloma.

(b) In the second case a benign fibroma containing areas of calcareous and myxomatous degeneration is described arising from a degenerative pannus.

A large number of mast cells are found in both growth and surrounding pannus tissue, and mast cell granules fill the protoplasm of many fibroblasts.

It is suggested that the agent producing the metaplasia may be a virus similar to the Shope fibromatous type in wild rabbits.

This suggestion is speculative, and without proof, as the idea of animal inoculation was a fruit of the histological investigation when it could no longer be carried out.

This must remain an unproved speculation, as the histological investigation which suggested it destroyed the material needed for the biological experiment which alone could have afforded proof.

Such cases should, therefore, in future be considered "*ab initio*" from the biological before the histological angle.

The amount of material required for injection into the anterior chamber of a rabbit (or better still a monkey) is so small that it need in no way prejudice the usual histological tests.

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## INTRA-OCULAR FOREIGN BODIES\*

An account of military cases from  
the Burma-Assam front

BY

E. J. SOMERSET and K. SEN

CALCUTTA

DURING 1944, 1945 and 1946, it was our privilege to operate upon a number of military personnel sent to the Eye Infirmary, Medical College Hospital, Calcutta, from the Indian Military Hospital and the British General Hospital, Calcutta. All but one of the cases described were battle casualties. The cases do not represent an unselected series of casualties. Only those cases showing two criteria were operated on by us. First, there was a retained intra-ocular foreign body, and secondly, at least perception of light with fair projection was present. Those cases in which vision was nil had been previously excluded, as also those cases of penetrating injury of the eye in which the foreign body was extra-ocular, though intra-orbital. It is thus a selected series of 29 cases which we are about to describe.

The most striking way in which these foreign bodies, produced by the fragmentation of modern war missiles, differ from foreign bodies due to the usual hammering and chipping accidents of civilian life, is in their magnetic properties. The former are usually very lowly magnetic while the latter are often highly magnetic. This was also the experience of Stallard (1944) during the North African campaign and during the later battles in France and Belgium: Stallard (1947).

Owing to the nature of the country and the extremely long and difficult line of communication, there was often considerable delay before we saw the cases. However, with the routine administration of the sulpha drugs by mouth at the Regimental Aid Posts, it was gratifying to see how few cases had become seriously infected. In fact, it would seem that it may even be an advantage for the cases to be treated conservatively for a few days, so that the eye can recover its tension before being subjected to operation. It seems that there is less likelihood of secondary haemorrhage if the eye has had several days rest. In any case the foreign bodies, being so lowly magnetic, very accurate localisation is necessary, so that the tip of the magnet may be placed as near to the foreign body as possible. With several weeks delay, however, there is the chance that the foreign body will become bound down by

\* Received for publication, June 11, 1947.

inflammatory fibroblastic reaction, so making extraction much more difficult.

There were 15 British cases, and 14 Gurkha and Indian cases. The only clinical difference between them, was that the Indian eye tends to settle down after operation or injury more rapidly than the British. While in the Army, one of us (E. J. S.), noticed the difference in cases in which there had been penetrating injury of the eye. If the eye was not quieting and settling down at the end of 14 days, but remained red, watery and irritable, one began to worry about sympathetic ophthalmitis. At the end of a further 10 days, most of the Indian and Gurkha cases had settled down and gave no further anxiety, while the British cases often continued to remain irritable for a further 10 days and the daily search for k.p. continued. In fact, no case of sympathetic inflammation was seen.

### Missiles

Table A shows the types of missile involved. Almost all gave a history of injury with a Japanese grenade. In most cases it would appear from the history that the explosion had taken place within a few yards of the soldier. All the foreign bodies were small, as might be expected. A large fragment so damages the

TABLE A

Missile	Number
Japanese Grenade ... ..	26
Japanese Mortar ... ..	2
Bomb Accident ... ..	1
Total ... ..	29

eye that perception of light is lost and the eye disorganised. The foreign body varied in size, from minute fragments less than 1 mm. in any diameter, up to 4.5 x 3 x 1.5 mm.

### Clinical facts

A careful history was taken and minute examination of the eye made, taking care to remember that even if one foreign body

was visible, there might be one or more others in the eye as well. Repeated fundus examination was made in case any foreign body had been missed in earlier examinations.

*Age incidence*—was as in Table B.

TABLE B

Less than 20 years	...	...	...	...	1
21 to 30 years	...	...	...	...	20
31 to 40 years	...	...	...	...	8

*Site of wound*.—The entry wound was through the cornea in 8 cases, at the limbus in 4, through the ciliary region in 8, through the sclera in 1, and could not be found in 8 cases. (Table C). A very small foreign body may penetrate the conjunctiva and sclera and leave no visible mark of entry. Nine cases were irritable and twenty were quiescent by the time they were sent to us. In only one case were k.p. present. This case refused enucleation and months later the foreign body was removed and he obtained 6/18 vision. The iris was torn or showed a hole in 6 cases, but showed posterior synechia in 7, and anterior synechia in 3 cases. The lens showed some signs of cataract in 14 cases—nearly 50 per cent. Table C shows the relationship between the site of the wound and

TABLE C

	Number	Associated Cataract
Through the cornea ...	8	7
At the limbus ...	4	2
Ciliary region ...	8	3
Not seen ...	8	2
Sclera ...	1	—
Total ...	29	14





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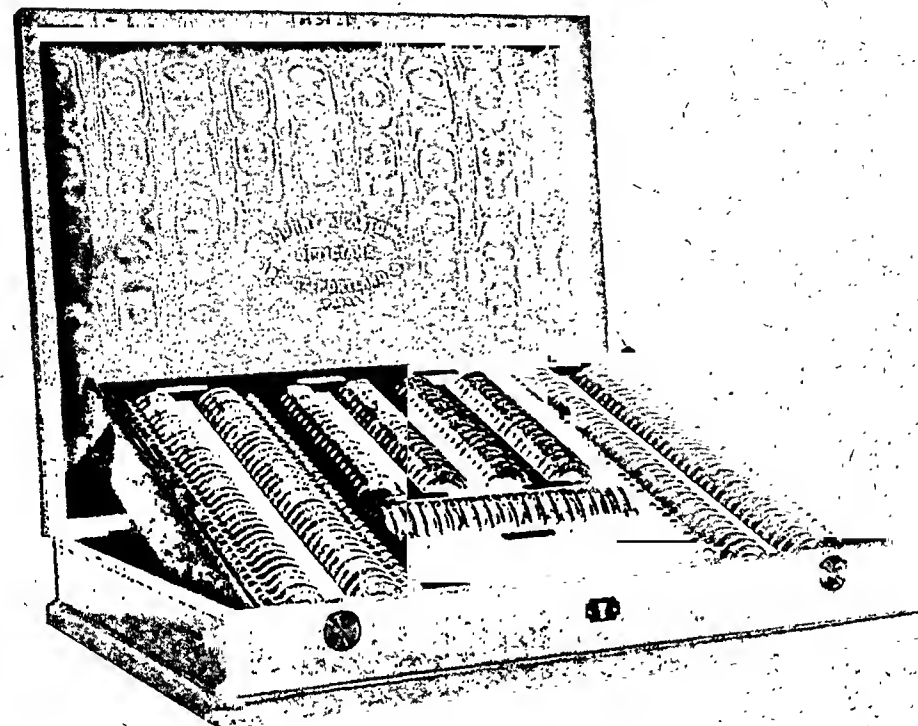


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haemorrhage in relation to the wound of entry. The incidence of vitreous haemorrhage is about 77 per cent, and is much higher than Stallard's cases in the B.L.A. series (44.4 per cent.) and the M.E.F. cases (48 per cent.), and in Scott and Michaelson's cases (1946).

*Vision.*—Vision before operation was as in Table E.

*Tension.*—In only 8 cases was the tension below normal to finger testing while the remaining 21 appeared to have normal tension by the time we saw them. No case showed a rise of tension.

*Retina.*—In 16 cases the retina was not visible on account of cataract or vitreous haemorrhage. In the other 13 cases there appeared to be retinal damage in 10 and 3 were probably normal.

*Multiple Foreign Bodies.*—There were 5 cases of multiple foreign body in the eye. In one case both were removed at one posterior route operation. In the second case of 3 intra-ocular foreign bodies, one came out at operation and two failed to come. This is counted as a failure. In the third case, there were 4 intra-ocular foreign bodies and only one could be extracted. In the fourth case, both foreign bodies failed to come out and in the fifth case, there was one foreign body in the left eye and two in the right. The foreign body failed to come out in the left eye, so no operation was attempted on the right. Posterior route operation was used in all these cases.

### Localisation

Before operation it is always necessary to know the exact position of the foreign body, so that one's incision can be planned accordingly. In 13 cases the foreign body could be seen with the ophthalmoscope. In all the other 16 cases, the ring method of localisation was employed. The method proved extremely accurate. The only disadvantage is that a small minor operation is required to sew the ring to the conjunctiva. The eye is anaesthetised with cocaine 4 per cent. drops and a ring 12 mm. in diameter made of thin silver wire is sewn with four silk sutures so that it accurately fits on the corneo-scleral junction. The sutures pass through the conjunctiva close to the limbus at 12 o'clock, 3 o'clock, 6 o'clock and 9 o'clock. A pad is placed on the eye and the patient taken to the X-ray department where an antero-posterior and lateral film of the orbit is taken. In every case, care is taken that the eyes are in the primary position. If the X-ray tube is 30 inches from the plate, little X-ray distortion of size occurs. The great advantage of this method is that the surgeon can see by looking at the X-ray picture whether the film

has been taken with the eye in the primary position, that is to say, the axis of the eye corresponds to the direction of the X-rays and at right angles to the plane of the film. With perfect centring, the ring will appear as a perfect circle in the antero-posterior view, and as a line in the lateral picture. If the eye has been turned away from the primary position during the exposure, the ring will appear as an oval and further pictures must be taken. The ring seen in the anterior-posterior film represents 12 mm. so that it is easy to draw on the film a circle twice the size, *i.e.*, representing 24 mm. diameter which must represent the circumference of the eye at the equator. The distance of the foreign body above or below and to the nasal or temporal side of the central corneal point can now be measured. Magnification of the ring on the film never amounts to more than 1 mm., and can be allowed for. In a similar way the distance of the foreign body behind the central corneal point can be measured from the lateral picture. In this way the foreign body is located in space relation to the central corneal point and so determination is made as to whether it is extra- or intra-ocular and estimation may be made as to the exact point on the sclera which is nearest to the foreign body.

For those cases in which the foreign body is near the sclera, some surgeons use two further pictures; one with the eye rotated up, and the other with the eye looking down. If the foreign body is in the globe, it will be seen to have moved with the eye. As one gets a somewhat similar movement of foreign bodies situated in Tenon's capsule, this added technique does not seem to us to be necessary or reliable. Figs. 1 and 2 show the position of 19 cases localised by X-ray. Of the remainder, one was in the

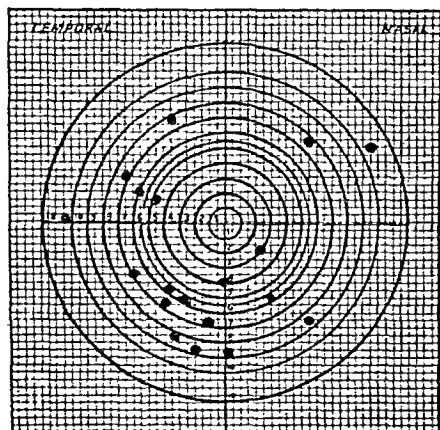


Fig. 1

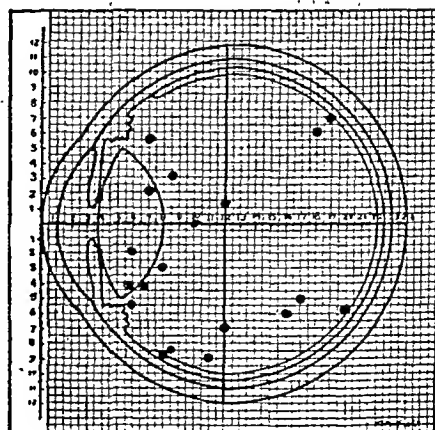


Fig. 2

anterior chamber and 9 were visible with the ophthalmoscope and so no X-ray was taken. How accurate the ring method of localisation can be is shown by the following case:

NAIK J.D.—Showed on examination: right eye vision equals perception of light, projection, nasal and inferior only. The eye was quiet. No wound of entry could be seen. Cornea was normal. Pupil was fully dilated with atropine. The lens was clear. The vitreous was full of blood and no fundus details could be seen. X-ray localisation showed one foreign body 13 mm. posteriorly, 13 mm. to the nasal side and 1 mm. below the horizontal. The foreign body therefore appeared to be outside the sclera, just behind the equator and underneath the internal rectus muscle. At operation the conjunctiva was incised and the internal rectus muscle exposed near the equator of the eye. The foreign body was removed with the tip of the No. 1 electrode of the Mellinger Magnet and was found to be lying under the muscle on the sclera, exactly in the position in which it had been localised.

### Magnet test

This was not of much value. It must of course be done before X-ray localisation. If done afterwards, it may cause the foreign body to take up a new position, thus nullifying the value of the localisation with X-ray. Very seldom was a pull obtained sufficient to cause pain or sensation. The foreign bodies are so slowly magnetic that they will only move slowly and gently to the sclera. If the foreign body is visible with the ophthalmoscope the magnet test will demonstrate whether the foreign body is magnetic or not. In several cases in which the foreign body was seen to move slightly forward towards the magnet on switching on the current, we were unable to manipulate it forwards into the anterior half of the vitreous. Thus anterior route extraction was impossible in many cases. They were subsequently removed by the posterior route. In two cases in which the foreign body was visible with the ophthalmoscope, the magnet test appeared to be negative and yet the foreign bodies were subsequently removed with the magnet by the posterior route.

### Choice of operation

Decision has to be made whether to extract the foreign body *via* the anterior route through a keratome incision in the cornea or, on the other hand, by the posterior route through a small incision in the sclera. In many cases the decision was not difficult as the

foreign bodies being so slightly magnetic it was impossible to draw them forwards to the iris and so through the pupil into the anterior chamber. It was thus essential to place the tip of the magnet as near to the foreign body as possible, so that the posterior route was inevitable. It is sometimes possible to bring a foreign body forwards through the pupil by repeated attempts each day, a procedure which is facilitated by repeatedly switching on and off the magnet some 20 or 30 times, Crawford (1943), Wright (1944). Care must be taken, however, not to overheat the magnet and we did not employ this technique except in those cases in which there was obviously a good chance of success. If we had burnt out our magnet there seemed no chance of repairing or replacing it for perhaps two years, which would have been a disaster.

### *Posterior route technique*

The eye was anaesthetised with 4 per cent. cocaine drops and a retrobulbar injection of 1.5 c.c. of 2 per cent. novocaine, and akinesia obtained by injecting the facial nerves with 2 per cent. novocaine, using the well-known O'Brien technique. The conjunctiva was incised concentrically with and about 1 cm. behind the limbus in the quadrant of the eye in which the foreign body was situated. The two recti muscles bounding the quadrant were exposed and retraction sutures placed under them. Thus if the foreign body was in the lower nasal quadrant the retraction sutures were placed under the inferior and medial recti. Throughout the operation a "no touch" technique was employed even to manipulating the lids with a swab stick when inserting the speculum. The sclera was cleaned with small swabs. The position of the ora serrata and the equator was marked on the sclera with a solution of methylene blue-gentian violet, applied with a Nettle-ship's dilator. The position on the sclera nearest to the foreign body was then marked. Five or six points of diathermy barrage were applied round this point, using Larssen's electrode. A fine thread scleral suture was inserted on either side of the marked point on the sclera so that it penetrated only the superficial half of the scleral fibres. The loop was left long so as not to interfere with the next stage. An incision was now made in the sclera with a Graefe knife between the scleral suture (Figure 3). This was usually 3 and never more than 4 mm. in length. The sclera was cut through gradually using repeated strokes so that the choroid was exposed. After this the choroid and retina were incised in a like manner so that the tip of the knife did not penetrate the vitreous. It may sometimes be possible to draw the foreign body through the retina without incising the latter with the knife, but

it is thought that more damage will be done to the retina in this way than that inflicted with the Graefe knife. The Mellinger magnet was then placed round the patient's head which was put in such a position that the incision was uppermost. No. 1 (the smallest) Mellinger electrode was now applied to the lips of the wound and the current switched on. If the foreign body failed to come out, larger electrodes were applied and the current switched on and off repeatedly. This would not always bring the foreign

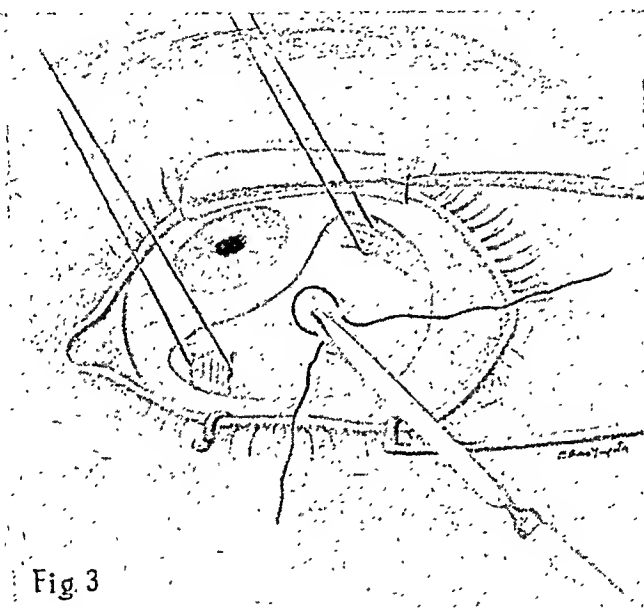


Fig 3

body out through the wound, in which case the smallest No. 1 electrode was again applied and was sometimes introduced 2 or 3 mm. through the wound. This was only necessitated when the foreign body had got stuck in the retina close to the incision. The scleral suture was then tied and cut short and the conjunctiva sutured.

### Results

Table F shows the results of the operation. In 6 anterior route operations, 5 were successful and one failed to come out. In this case there had been an iris prolapse excised in the forward area and the foreign body was localised to be lying behind the iris near the ciliary body. It proved to be either non-magnetic or bound down by organised fibrous tissue.



In 23 posterior route operations the foreign body was extracted in 17 cases, and in 6 cases it failed to come out. Thus in 29 operations the foreign body was removed in 22 with 7 failures. This gives 75.8 per cent. of extractions. With multiple intra-ocular foreign bodies, unless all came out the case was recorded as a failure.

TABLE F

	Jap grenade	Jap mortar	Bomb accident	Total
POSTERIOR ROUTE				
Magnet extraction ... ..	14	1	—	15
*Non-magnetic extraction ...	2	—	—	2
Not extracted... ..	6	—	—	6
ANTERIOR ROUTE				
Magnetic extraction ... ..	3	1	1	5
Not extracted... ..	1	—	—	1
Total ... ..	26	2	1	29

\* These foreign bodies came out on incision of the sclera.

In one case of anterior route extraction the eye continued to be irritable and was enucleated. One case, in which there was extensive vitreous haemorrhage, subsequently developed many vitreous bands and detachment of the retina supervened. One case after posterior route extraction developed a detachment of the retina below the area of diathermy barrage which could be clearly seen. In spite of complete rest in bed and stenopaic goggles the detachment was seen to be extending and so was operated upon successfully, the retina going back into place with retention of 6/6 vision. No case developed a post-operative infection. Most of the cases were only retained in the Eye Infirmary, Calcutta, for about three weeks after operation, so that observation of late visual results was impossible.

*Vision.*—At about 3 to 4 weeks after operation, visual acuity was unaltered in 17 cases. In 8 vision had improved, and in 4 it was worse. These four included one eye which had had perception of

light only and was subsequently enucleated for continued irritation, and one whose vision had fallen from poor projection to nil. The remaining two showed some increase in the vitreous haemorrhage, although diathermy barrage had been used at operation.

### Summary

A description of 29 cases of intra-ocular foreign bodies mostly from Japanese grenades in the Assam-Burma Front is given.

The low-magnetic properties of the fragments necessitated posterior route extraction in most cases.

Ring X-ray localisation proved very accurate and the Haab test was of little value and often misleading.

The main causes of visual defect were vitreous haemorrhage and cataract.

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## SOLAR RETINITIS\*

BY

EMANUEL ROSEN, M.D.

NEWARK, N.J.

In January, 1943, C. A. Pittar reported a rather unusual case of "hole in the macula" following indirect "sun gazing." The case assumed military as well as medico-legal importance for the pertinent data in the case report indicate that complete loss of vision was "in line of duty." The history obtained from the patient one and one half years after the acquisition revealed the fact that enemy planes had a habit of flying out of the sun, and being in charge of an anti-aircraft gun he had upon several occasions looked into the sun. He could not clearly recall one specific instance when he had gazed into the sun. The patient's record revealed that two years earlier he had had perfectly normal vision in each eye. Another record indicated that at the time of examination for a cinder in his right eye the ophthalmologist had noted "clouding of the macula along with pigmentation and

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haziness." There was at this time almost complete blurring of vision for three weeks' duration and a history of "sun exposure" was recalled.

In reconstructing the picture the following facts seem to stand out :

- (a) The sailor had had 20/20 vision in each eye.
- (b) Some time after watching planes fly out of the sun, a central scotoma developed with loss of vision for a period of three weeks. At this same time a cinder was present in the patient's eye.
- (c) Fundus examination showed a picture typical of "solar retinitis," but it was mis-diagnosed and explained as corneal involvement.

(d) One and a half years later a typical macular hole was found in the right eye with vision of 2/60.

The author quotes Duke-Elder and states that no other single reference "of typical hole in the macula due to exposure to sunlight" has been reported. He analyses the three cases cited by Duke-Elder of other authors, *viz.*, Würdemann, Harmon and McDonald and Rauh, showing that these cases are not photo-traumatic holes in the macula since they were caused by other elements. Würdemann's case report was not one of eclipse blindness but hole production in the macula in a patient who looked into a welding flash for two to four minutes. This patient was a myopic female (-6.0 dioptres). A typical "Berlin opacity" of the macula was reported along with multiple radial macular haemorrhages. Later the macula developed a greenish cast with a whitish centre. The final appearance was a typical hole in the macula. The author placed emphasis upon the fact that only a few seconds' exposure will destroy the delicate system of nerve elements in the macula. The author also believes the process in sun gazing, electricity, lighting, etc., is very similar. The appearance of this lesion is not unlike that described in our first case, *viz.*, the "yögi sun gazer."

In Harmon and McDonald's case, no true hole in the macula was observed, rather a retinal detachment developed which was subsequently followed by striation and scarring in the macula but not hole formation.

In October, 1943, I had the extreme good fortune to examine a patient who apparently fitted into the pattern described by C. A. Pittar. This patient was a 24-year-old Mexican who stated that he directed his gaze into the sun and maintained fixation constantly for a period of fifteen to twenty-five minutes. He also stated that at first the sun appeared as a complete blur with no visible structure but after a short period its shape could gradually be made out.

For three days following this act, the patient noticed a large round black spot in front of each eye. In time this spot became smaller in diameter and after one week the scotomata continued to maintain a constant size. At present the spots are round upon direct visual localisation.

The patient's vision was 20/100 in each eye and could not be further corrected. The initial fundus examination, which was made about six weeks after this episode, showed each macula to have a peculiar greenish colour with a pigment halo following just around the foveal reflex. Anterior to the foveal depression in each eye was a small whitish grey fluffy area. This looked very much like a "powder puff" being somewhat transparent and allowing a slightly translucent glow when viewed by retro-illumination (method of Friedenwald). This picture was more or less bilaterally symmetrical. When re-examined ten days later the "puffs" had disappeared and each macula had taken on an increasingly darkened area. Five weeks later it was noted that a definite hole had appeared in each macula. These holes were rather small yet cleanly punched out and girdled by a pigment halo. In another two weeks each hole appeared oval horizontally with a pronounced pigmentary ring. There was little change in this picture in the next six weeks.

While obtaining the patient's history I had casually mentioned to one of the medical men that "sun gazing" was frequently practised in India as a religious ritual. I asked the patient if he had ever practised yogyism. This he denied. Sometime later I read the following in Elliot's Tropical Ophthalmology :

"Sun-blindness, with macular degeneration, is not uncommonly met with, and the ophthalmoscopic picture is quite characteristic. The macula forms a crater of deep crimson colour,  $1/8$  disc diameter in width, the edges of which are sharply cut and irregular in shape; it is surrounded by a soft cloud of pigment.

"In this connection, it is interesting to note that it is part of the Brahmin ritual to look at the sun whilst reciting a particular 'mantram' during the mid-day prayer. The practice is to fold the fingers in a peculiar manner, and look at the sun through the interspaces. The orthodox fashion of dodging the fingers leaves an aperture of about an inch square, but it seems that all Brahmins are not equally particular as to the manner of folding the hands; indeed, some of them do not even go outside the house to perform the rite, but are content to take the presence of the sun for granted, and merely to address the light. The mantram itself only takes three or four seconds to recite but one may imagine that the tropical sun, if looked at directly, is capable of doing damage, even in this short space of time. In some places it appears to be

the custom to look at the rising sun directly, without the intervention of the fingers, and in such a case the time may be extended to four or five minutes. It is remarkable that this disease is by no means confined to Brahmins; indeed those who are not Brahmins have furnished the majority of the patients. The probable explanation is that this practice, having a religious sanction, is followed by men of other castes, and that these imitators are inclined to carry it to excess; it is sometimes considered to be "lucky" and to confer supernatural powers. This idea most likely originates in the extensive use of self-hypnotism by "yogis," who, for this purpose, are in the habit of fixing a sustained gaze on some bright object, or of using their eyes in some manner which entails a fatigue of the ocular muscles. Thus a common yogi habit is to gaze at the tip of the nose or at the eyebrows, the power of sustained over-convergence, which they thus acquire, is, in some cases, astonishing. Sun-gazing in the morning and evening appears to be one of the methods of self-hypnotism. Amongst the less zealous worshippers the disease is often monocular, as some, at least, of them appear to have a doubt as to the wisdom of tampering with such things, and, tempering their zeal with discretion, risk the sight of one eye only. On the whole it is extraordinary that sun-blindness is not more common than it is."

In October, 1943, L. Pavia and Lachman described two cases of very small holes in the maculae due to photo-traumatism. These authors describe three types of "solar" injury and they show three fundus photographs with typical macular holes. One case was unilateral, the second bilateral. In each case the history was typical, *i.e.*, an eclipse was observed with no apparent protective measures. There was sudden loss of vision with gradual restoration after a period of days—but not complete restoration. The patients were not examined until several years later, at which time typical macular holes were found. The unilateral case was complicated by an endocrine dysfunction.

Pavia and Lachman review the literature and state that most authors stress the oedema, clouding and pigmentation which occur in the macula with little emphasis being placed upon the final macular picture. Animal experimentation was quoted to show the nature of the pathological lesion in the macula concerning which changes some controversial opinions had arisen. However, in the last analysis the anatomical difference of man and animal, particularly in the macular region, was stressed.

The human experiments of Maggiore did not enlighten the picture very much either, since this author used primarily an artificial light source at a very near distance. In conclusion,

Pavia and Lachman emphasise the patient's refraction; the distance of the source of light; the intensity of the light and the interval of time before examination to explain the occurrence of the small macular holes.

In the past year I have had occasion to observe a great many cases, during routine examination, which showed these small, easily overlooked macular holes. When discovered I have checked back upon the patient's history, trying not to ask leading questions and in all cases I have elicited a history of "sun-gazing" or a related act. In most instances these patients recall with facility all the events accompanying the act of sun-gazing. A prepared table includes many of the methods and some of the protective procedures followed by these patients.

Review of these cases seems to indicate that many patients recall gazing into an eclipse through self smoked glasses. In many cases one eye was covered for protection. The macular holes were of a very small variety. In some instances the method of development was rather peculiar, such as gazing into a stream of water, a water pail or looking through a self-made stenopaeic slit. The time interval varied from five minutes to an hour and a half. One patient believed that the eye became strong through gazing into the sun. He had come to believe through folk lore or some local teaching, that to become "eagle eyed" one must gaze into the sun even as the eagle does. In other cases the patient stated that he along with other boys gazed into the sun for several minutes and that many of those in this same group suffered from similar ocular troubles years later. One patient (No. 12) not only looked at the sun through smoked glasses for several minutes but also used to study the sun through a telescope. His cousin also had an eye complaint very much like his and had sought ocular aid without benefit.

In 1944, H. E. Smith reviewed 150 cases in military personnel stationed in a tropical country. These were men whose visual acuity had been previously recorded by this same observer. They were subsequently exposed to tropical sun, working out doors, etc. After a period of six months it was noted that these men had fallen in vision from 20/20 to 20/30 and that this vision could not be improved through refraction. The author noted that in each case the fundus lesion was more or less typical regarding macular disturbance. He described three fundus patterns which were very constant. Smith pointed out that these men worked at all times in the bright sunlight—being unprotected from glare and for the most part not used to this strength of sunlight. The author did not discuss the pigmentation of these men, nor the prophylactic measures taken against the strong sun nor the subsequent and

No.	Initials	Age	Vision O.D. O.S.	Type of Exposure	No. yrs. ago	Protection	RX	Nerve	Macula	Retina
1	P.	22	20/100 20/100	Constant sun gazing 15-25 min.	2 mths.	None	—	—	Hole	Neg. hole
2	C.	26	20/100 20/20	Sun gazing for several min.	13 yrs.	Smoked glasses	—	Norm.	Hole	Neg.
3	J. J.	20	20/200 20/100	Watched sun in a "water bucket"	15 yrs.	None; no eye closure	+ 1.50	Neg.	Holes	Neg.
4	H. W.	24	10/200 20/50	Watched sun for 1 hr.	7 yrs.	None	+ 1.50	Neg.	Hole	Neg.
5	V. H.	25	20/20 20/100	Watched sun for 1½ hrs.	5 yrs.	Doesn't recall events	+ 1.00	Neg.	Double Hole	Neg.
6	S. C.	25	20/20 20/100	Watched sun for ½ hr.	14 yrs.	Closed left eye	+ 1.00	Neg.	Hole	Neg.
7	J. T.	36	20/70 20/100	Watched sun for ½ hr.	20 yrs.	Closed right eye	—	Neg.	Hole	Neg.
8	J. L.	22	20/20 20/20	Watched eclipse for 3 min.	6 yrs.	None	—	Neg.	Hole (small)	Neg.
9	S. C.	26	20/40 20/40	—	6 mths.	None	—	Neg.	Hole	Neg.
10	R. M.	25	20/40 20/30	Sun gazing for 15 min.	15 yrs.	Covered left eye	- 0.25	Neg.	Hole (small)	Neg.
11	A. S.	23	8/200 20/20	Gazed at sun 3-5 min.	15 yrs.	None	—	—	Pigment around macula — small hole	—
12	M.	21	20/200 20/30	Gazed at eclipse 15 min.	2 yrs.	Smoked glass	+ 0.25	Neg.	Hole	Neg.
13	A.	26	20/30 20/30	Looked into stream many min.	6 yrs.	None	+ 0.25	Neg.	Hole	Neg.
14	D.	29	20/30 20/70	Sun gazing 1 hr.	8 yrs.	None	+ 0.75	Neg.	Holes	Neg.
15	J. B.	28	20/70 20/20	Sun gazing in stream (eclipse)	9 yrs.	None	+ 0.50	Neg.	Hole	Neg.
16	C. E.	33	20/20 20/20	Sun gazing for 5 min.	12 yrs.	Closed left eye, smoked glass	+ 1.25	Neg.	Hole	Neg.
17	J. P.	27	L.P. 20/20	Sun gazing for 30 min.	12 yrs.	None	+ 1.25	Neg.	Hole	Neg.
18	G. S.	23	L.P. 20/30	Sun gazing for 45 min.	10 yrs.	Closed O.S.	—	Neg.	Hole	Neg.
19	T. G.	24	20/180 20/60	Watched eclipse for 15 min.	14 yrs.	None	—	Neg.	Hole	Neg.
20	H. H.	23	20/25 20/20	Watched sun for 15 min.	12 yrs.	Small hole in cardboard. Cov. O.S.	- 4.00	Neg.	Seg. & hole O.D.	Neg.
21	H.	24	20/70 20/20	Watched sun for 4-5 min.	15 yrs.	None	- 4.00	Neg.	Hole (small)	Neg.
22	M. H.	—	20/40 20/25	Gazed on reflecting white surface several mins.	8 mths.	None	—	Neg.	2 small holes	Neg.
23	G.	24	20/70 20/25	Watched eclipse 5 min.	1½ yrs.	None	—	Neg.	Small biconvex hole	Neg.
						Through opening in hand	—	Neg.	Bilateral holes	—

final course of the macular lesion (probably as yet too early). However, these case reports seem to bridge the gap between the many descriptions of the acute oedema following eclipse blindness and the ultimate small macular holes found many years later. Since the condition is far from rare and since the problem is largely one of prevention, it is urged that this subject be placed before many who are unaware of the dangers of "sun-gazing." That the danger is not recognised by ophthalmologist as well as by the unsuspecting sun worshipper may be readily realised when one quotes directly from Troncoso's text book upon Internal Diseases of the Eye and Atlas of Ophthalmoscopy (page 382).

"The use of smoked glasses during sun eclipses will prevent injury to the retina."

Case 23 is an excellent example of the medico-legal importance of this condition. This man had vision of 20/20 in each eye at the induction examination. One and a half years ago while he was stationed in Alaska he gazed at an eclipse for five minutes through a small opening made by his own hand. He used one eye and then the other. There were no immediate after effects. At present his vision is 20/70 in his right and 20/50 in his left. There are holes in each macula to correspond with the vision of each eye. The causal relationship seems quite clear in this case. The problem of education along preventive medical lines seems almost as glaring.

### Report of cases

CASE 1.—The patient is the above-mentioned Mexican, aged 24 years, who gazed constantly at the sun for a period of 15 to 20 minutes and developed the several changes which we followed and described in an earlier paragraph.

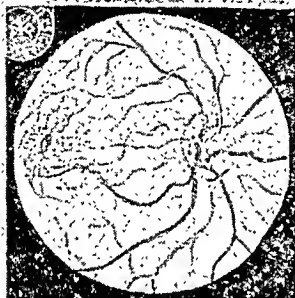
CASE 2.—This is the case of a soldier, aged 26 years, whose vision was 20/100 in the right eye and 20/20 in the left eye, no improvement being obtained upon refraction. In the right macula a very small "kidney bean" hole was present with the long axis lying horizontal, and a lighter halo surrounding the small hole. There was some increased pigmentation beyond this point. The nerve head and fundus otherwise was normal, as was the fundus of the left eye. The patient recalled that thirteen years earlier he had observed an eclipse at which time he had smoked a piece of glass and had gazed intently at the sun while keeping his left eye closed. When he returned for a second examination he was able to recall that his right eye had remained blurred for a few days following the "sun gazing." At first quite a definite golden ball was present, but this gradually disappeared, although not completely. He had done nothing about this condition and had never connected his poor central vision in his right eye with this episode of sun gazing. He knows that although he is right handed, he has learned to use his left eye as his dominant one.

CASE 3.—This patient, J.E.J., aged 20 years, stated that when he was six or seven years old he had watched the structure of the sun through reflection into a bucket of water as part of a religious ritual. He does not remember how long he gazed into the bucket of water nor how long his eyes were troubled as a result of this procedure, but he does remember that he had a good deal of discomfort following this episode. He had had his vision checked at school upon many occasions, but had never been given any glasses. The right fundus showed a



tiny hole in the foveal area, quite dark, undermined and horizontally elongated. The hole in the left macula was slightly smaller, also horizontally elongated with a surrounding pigment halo and two small dots of yellowish colour at its centre. (Case 3.) The retinae otherwise were negative. Central fields showed two small absolute scotomata corresponding in size and shape to the original lesion.

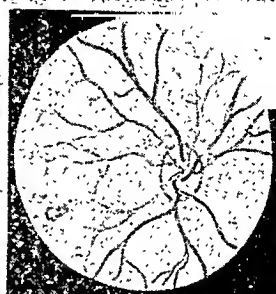
CASE 4.—This soldier, aged 24 years, recalls watching an eclipse without any protective mechanism other than self-smoked glasses for a period close to one hour when he was 17 years of age. He well remembers the after-effects, for he was unable to read print for three or four days because of a constant dazzle in front



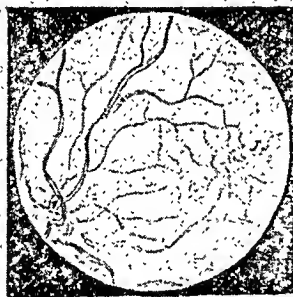
CASE XI



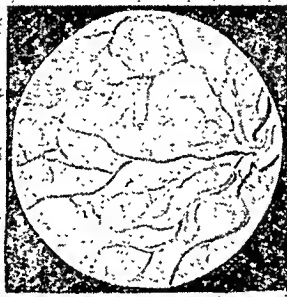
CASE XII



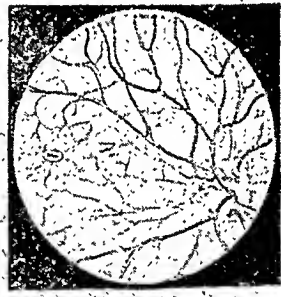
CASE X



CASE III



CASE IV



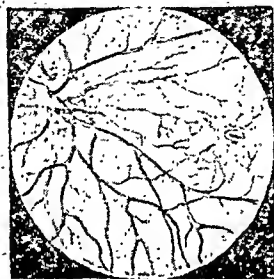
CASE II

of his eyes during this period. This effect gradually disappeared at the end of one week, although his right eye thereafter seemed to have a permanent blank area when looking straight ahead. He did not have this condition investigated at the onset, although he tried later to secure glasses without benefit. Examination of the fundi showed a small macular hole in each eye very similar to the "hole" seen in Case 3. Here also were two small round yellowish spots at the base of the hole which ran in a horizontal plane and had a small yellowish lighter halo about the very dark red punched-out centre. The right macular hole was somewhat larger and more oval than the left hole. Vision in this patient's right eye was 20/400 and in the left eye was 20/50, uncorrectable.

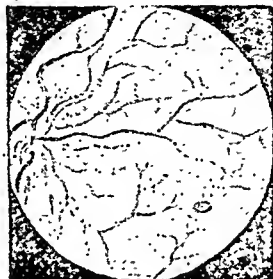
CASE 5.—This male, aged 25 years, had vision of 20/100 in the right eye and 20/20 in his left eye, not improved with glasses. On checking the patient's history he was able to recall watching a sun eclipse through self-smoked glasses for a period well over an hour, during which time he remembered keeping his left eye closed. He doesn't remember the exact effect this had upon his eyes other than

that he was very uncomfortable for several days thereafter. He had completely forgotten this experience, and in no way did he connect it with his poor vision in the right eye. Examination of the fundus of the left eye was not abnormal; that of the right showed a peculiarly shaped spindle-like hole with a dark symmetrical ring around the spindle. Increased pigmentation could be seen around this area. The fundus otherwise was negative. A central defect corresponding to this hole in shape and position was mapped out upon the tangent screen.

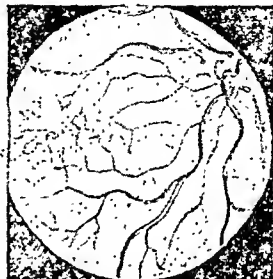
CASE 6.—T.J., a male, aged 36 years, had vision of 20/70 in his right eye correctible to 20/20, and 20/100 in his left eye—uncorrectable. Twenty years earlier he had watched an eclipse for a period of one hour and at that time



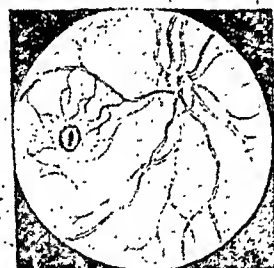
CASE VI



CASE VIII



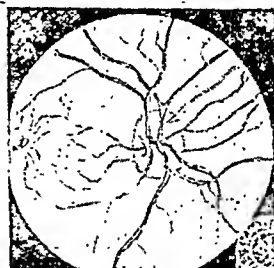
CASE VII



CASE IX



CASE V



CASE IX

distinctly remembers closing his right eye. He believes he gazed at the sun for a period of one-half hour and that for several days thereafter his vision was quite blurred, remaining that way. The right fundus showed no abnormality. The left fundus presented a characteristic macular lesion consisting of a minute macular retort-like lesion running horizontally and being surrounded by a definitely lighter halo outside which was an area of increased pigmentation extending for a distance equivalent to one disc in diameter.

CASE 7.—Although this male, aged 22 years, had vision of 20/20 in each eye, yet a very tiny hole was discovered in his right eye. He recalls gazing into an eclipse when he was about 12 years old. He believes his left eye was covered at the time, but doesn't recall that he used any protective method. At most he believes his gaze was directed toward the sun for a period of three minutes. He was not aware of any after images or immediate visual disturbance. Examination of his right fundus disclosed a very small dark red macular lesion, more or less oval in shape with two small yellow dots within its centre. There was a slight suggestion of a halo around the hole and a small zone of increased pigmentation. The left fundus was normal.

CASE 8.—This adult, aged 26 years, had vision of 20/40 in each eye which could not be improved. Examination of his fundi showed bilateral hole formation, the right eye being multiple (Fig. 5, Case 8), the left eye being single, obliquely oval

and heavily pigmented. Fig. 5 shows the right macular lesion consisting of three very tiny separate holes, one being crescentic, one being circular and the third being very small and shaped like a figure 8. The retina between the holes was very shiny and almost silvery. The central lesions were surrounded by a circle of small pin point dots, with the area showing increased pigmentation. The crescentic lesion appeared deepest; the circular lesion had a yellowish centre. No history of sun gazing or eclipse viewing could be obtained from this patient who insisted that he had developed his eye trouble while upon desert manoeuvres during the past six months during which time he had been troubled by the reflection of the sun from the desert sand.

CASE 9.—This patient, aged 25 years, gave a definite history of gazing into the sun at the age of eleven for a period of fifteen minutes, his left eye being closed and his right eye viewing the sun through a smoked glass. There was a definite visual aftermath, although the patient doesn't remember any of the details. At present vision is 20/40 in his right eye and 20/30 in his left eye in which eye vision can be corrected to 20/20. The right macula shows a very small "banana" shaped hole with two polar yellow dots and a discrete circum-macular halo. The central field showed a very minute defect corresponding to this macular lesion.

CASE 10.—The patient stated that vision in his right eye was poor as long as he can remember. Vision in this eye is 8/200, in the left eye 20/20. Upon further questioning he admitted that when he was seven years of age he had observed an eclipse without protecting his eyes. He believes that he watched the phenomenon for at least five minutes. However, he cannot describe any subsequent ocular symptoms. The left fundus appeared to be perfectly normal. The right fundus showed a small hour glass, punched out, dark macular hole with two small round yellowish dots. There was no halo around this lesion although there was an area of increased pigmentation extending about the macular lesion as large as one disc's diameter.

CASE 11.—U.A., aged 26 years, had vision of 20/30 in each eye. About six years ago he had carefully studied "sun spots" by gazing into a stream steadily for several minutes. His vision following this procedure has not been as good as it was prior to this experiment. He had tried to secure glasses to correct this visual defect on several occasions but was never fitted satisfactorily. Case 11 shows a typical macular lesion shaped like a spindle running in the vertical direction with a small whitish-yellow dot in the centre. The lesion is typically punched out and is surrounded by a girdle of very small dark dots along with an included area of increased pigmentation. The left eye is very similar to this right eye. There is no other fundus pathology. The central fields show typical central scotomata.

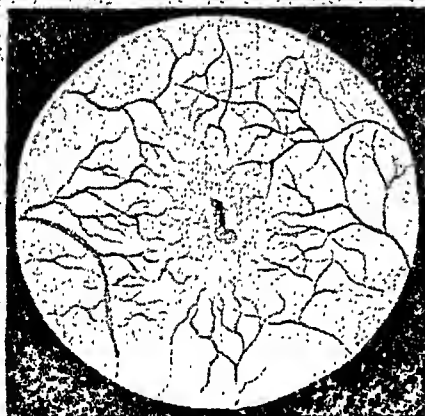
CASE 12.—This patient, aged 21 years, had vision of 20/200 in his right eye and 20/30 in his left eye. When he was eighteen years of age he had watched an eclipse both through smoked glasses and through a telescope in an endeavour to study the phenomenon. In watching the sun a smoked glass was used over his eye as well as over the telescope. The history of visual disturbance following this procedure was very precise; in fact, the patient knows that others who viewed the eclipse through this telescope also have developed some form of "eye trouble." The right fundus shows a very definite hole made up of two components as shown in the illustration Case 12. This hole is not dark red, but has a definite punched-out appearance along with an area of increased pigmentation. The left fundus is normal.

CASE 13.—This soldier, aged 29 years, recalls gazing at an eclipse when 21 years of age, using both eyes with no manner of protection other than carbon deposition upon a broken piece of glass. Again the exact time interval is not known, but it is the patient's belief that possibly a whole hour was consumed in this nefarious procedure. Visual impairment was immediate and definite, and at present is 20/30 in the right eye and 20/70 in the left eye, no further improvement being obtainable. There is only a slight hyperopic correction in each eye. Although there is a marked visual difference in each eye, the lesions in each macula are fairly similar: The figure, Case 13, illustrates the appearance of the lesion in the left eye which is very similar to the lesion depicted in Case 7.

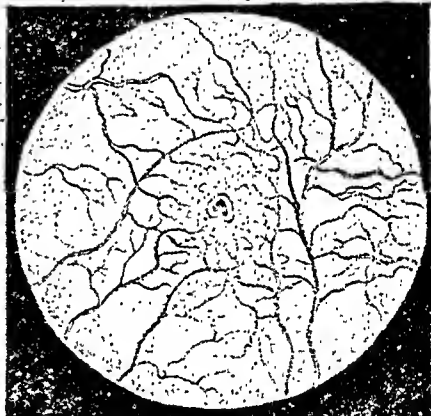
CASE 14.—This patient observed an eclipse of the sun by gazing into a stream

when he was 19 years old. This incident occurred nine years ago at which time no smoked glass or other device was used. Both eyes were kept open during the phenomenon, which lasted some five minutes, and was completely observed by the patient. This was followed by bilateral central scotomata which persisted for several days and gradually but incompletely disappeared. No medical aid was sought, for vision returned to its present status of 20/30 right, and 20/70 left, no further improvement being secured through attempted refraction. The hole in the left eye is illustrated in Fig., Case 14. There is a vertical, rather minute, punched-out hole shaped like an italic letter (o), surrounded by a very definite lighter halo, and an area of markedly increased pigmentation. A very definite central scotoma is present in each eye.

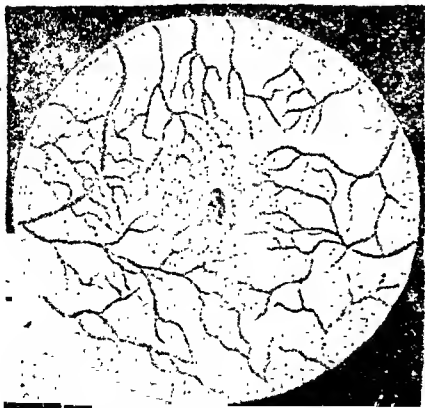
CASE 15.—This patient, C.E., aged 33 years, recalls gazing at an eclipse 12 years ago through a self-smoked glass while keeping his left eye closed. After five minutes he discontinued the process. He noticed that a blur persisted in front of his right eye which did not vanish, although it became much less intense after several days. He was particularly annoyed while sighting through a rifle, noting that he could sight much better slightly off centre. These symptoms have persisted ever since. Examination of the right macula showed an inverted heart shaped lesion with a halo around it, and area of increased pigmentation around



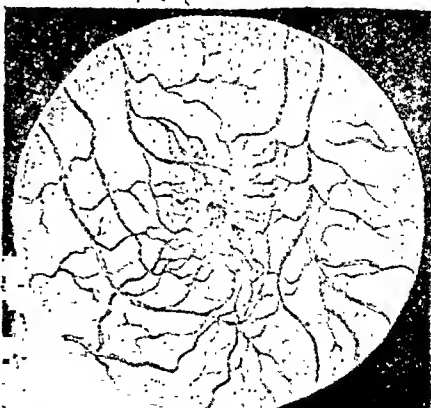
CASE XIV



CASE XV



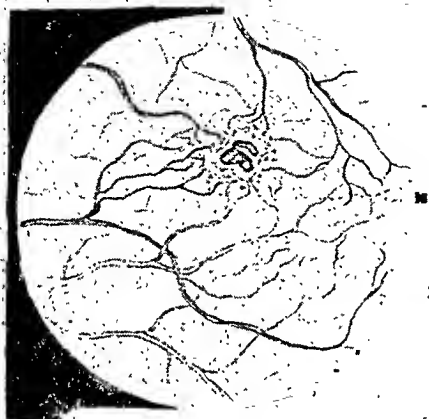
CASE XVI



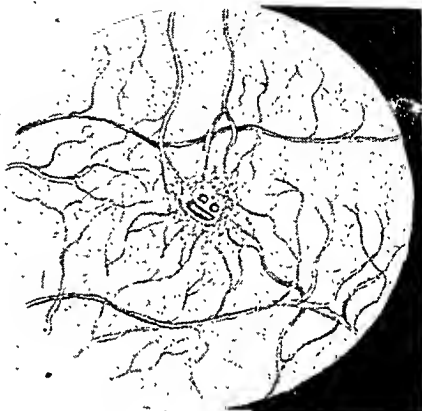
CASE XVII

the foveolar area. There was a small central scotoma in this eye. The fundus of the left eye was quite normal.

CASE 16.—J.P., aged 15 years, had gazed upon a sun eclipse for fully twenty minutes through his right eye with no form of protective glass. There was immediate loss of vision which persisted for several days, gradually clearing somewhat, but remaining approximately 20/400, although the patient claimed he could see nothing more than large objects with his right eye. There were no signs or symptoms referable to his left eye. Examination of the right fundus



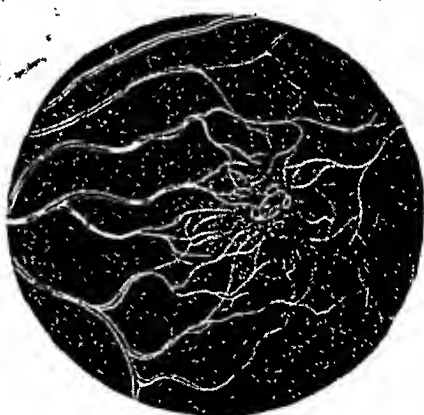
CASE XVIII



CASE XIX



CASE XX



CASE XXI

showed a moderately large, dark hole shaped like a hammer head and running vertically. It, too, was surrounded by a halo of lighter than normal retinal tissue, along with an area of increased pigmentation which occupied a region as large as one disc's diameter. There was a large central scotoma to correspond with the macular defect.

CASE 17.—When this soldier, aged 23 years, was 13 years old, he had watched an eclipse with his right eye for a period close to half an hour, keeping his left eye closed, and not using any protective method over his right eye. Vision at present was 20/400 in the right eye and 20/30 in his left eye. Although a

disturbing after-image existed after this experience, the patient had never investigated the cause of his visual impairment, just disregarding vision in his right eye and using his left for central fixation. Examination of the right fundus showed a comma shaped small hole of punched out character with a series of three conjoined smaller holes lying just nasally and below. There was no pronounced halo or depigmentation phenomenon.

CASES 18, 19, 20 and 21 are all cases of gazing into an eclipse at approximately 12—15 years of age, closing one eye and looking through self-smoked glasses. Case 20 varied the procedure by gazing through a stenopaic slit in a cardboard. The time interval of exposure varied from five to twenty minutes. The macular lesions consisted of small polymorphous and multiple holes, surrounded by a halo and containing small yellowish central spots within the holes. In each case the story was the same—an eclipse was viewed through self-smoked glasses, keeping one eye closed and becoming aware of a distinct visual disturbance subsequently, which for one reason or another was not investigated or explained.

CASE 22.—This soldier had lived in Idaho all his life and he was able to recall several "bouts" of so-called snow-blindness, which he experienced in his early childhood. These were bilateral, acute episodes, associated with excessive photophobia, tearing and smarting, which usually lasted for several days during which time the patient was unable to see very well. He had regarded these attacks as typical cases of snow-blindness and thought very little about them. He also recalled many instances in his early life of watching the sun and viewing an eclipse through smoked glasses, although he is not very familiar with any symptoms which may have followed these experiences. There were many occasions, too, in which he had exposed his eyes to the direct rays of the acetylene welding torch, but cannot remember that any harm was produced by such an act. Upon induction his vision was found to be 20/20 in each eye. About eight months ago while in Alaska and while working outdoors he fixed his gaze upon a reflecting white surface for several minutes, and thereafter experienced an after-image of golden yellow in each eye which persisted for more than a week and was associated with intense tearing, blepharospasm and burning. At first he thought these symptoms were similar to those he had experienced in his early youth in Idaho, but when these symptoms left a permanent defect in his vision he felt that something further had developed. He did not seek aid until his return to the United States about one month ago, at which time his fundi revealed bilateral typical macular holes of small calibre with surrounding halos. Vision in the right eye was 20/40 and in the left eye 20/25. The hole in the right eye resembled the map of India in shape, that of the left eye was much smaller. Scotomata were present in both eyes. In the right eye besides a central lesion there was a pronounced downward elongation of the blind spot.

Since writing the above paper an excellent article has appeared by D. O. Harrington in the *American Journal of Ophthalmology* (Vol. XXIX, No. 11, November, 1946, p. 1405) on "the autonomic nervous system in eye disease," in which the subject of "solar retinitis" is taken up. This author concludes that cases of this sort are unusual and that "these lesions are thought to be the results of localised vasospasm of retinal arterioles and capillaries in the macula initiated by thermal or infra-red rays and terminating in a small hole." From his conclusions I believe Harrington indicates that this end result is part of the clinical picture of a "vaso-neurotic diathesis in an autonomically unstable person." To this conclusion I would like to add just one fact—namely that I have observed over 500 cases of these small macular holes in "coloured" troops, none of whom were vaso-neurotic and every-one of whom was exposed to the direct action of the sun's rays.

## ON RESULTS OBTAINED BY TOTAL CONJUNCTIVAL HOODING OF THE CORNEA FOR SERPIGINOUS ULCER

BY

Prof. A. KETTESY

DEBRECEN

It is more than 5 years since I introduced a new surgical proceeding for treatment of serpiginous ulcer. The results are so satisfying, that it seems to be worth while to call attention to it.

The operation was devised in 1927 for a case of intractable Mooren's ulcer, and published in 1933, having healed three cases of this so far incurable disease.

The proceeding consists of covering the whole cornea by a conjunctival flap, instillation of cocaine and subconjunctival injection of novocaine and adrenalin in order to raise the bulbar conjunctiva. The bulbar conjunctiva is detached by circumcising it all around the limbus. It is undermined into the upper fornix.

After having scraped the ulcerated parts of the cornea with a Meyhöfer spoon, the round hole in the conjunctiva is united by "anchoring" cat-gut sutures in an almost horizontal line below the cornea.

"Anchoring" means the sutures take up some episcleral tissue. We put in the first suture at 6 o'clock. After having passed the needle through the upper conjunctival edge, we grasp the inferior rectus (in order to fix the eye-ball), then take up some episcleral tissue horizontally 3 mm. below the cornea and bring the suture out through the lower edge of the conjunctiva. It is advisable to use a corneal needle. Thus the line of suture is fixed below the cornea, an important condition of the success, as this is the only way to ensure against spontaneous reopening of the wound.

In cases of Mooren's ulcer the cornea remained covered one year. Then a little hole was made into the middle, behind which the clear cornea reappeared and the patient could see again.

I was led to this solution by the inefficacy of Kuhnt's partial conjunctivo-plasty. The partial hooding always retracts too quickly before a firm coalescence between conjunctiva and flap could have taken place. The ulcerated margin reappears in a few weeks and the disease progresses further.

One of my assistant-surgeons seeing the satisfying results of Mooren's ulcers, proposed in 1940 to try the proceeding in refractory

cases of serpiginous ulcer too. Two years later we were able to publish already the results of 25 cases. Since that time this proceeding is a systematic method of my clinic. As far as I know, it has not yet been accepted elsewhere, except by Lawaetz, who reported 6 successful cases in the Danish Ophthalmological Society in the year 1943. Although Meisner mentions it in the recent German text-book of ophthalmic surgery edited by Thiel (1942, p. 242), there are misunderstandings in the text as well as in the figure and it is evident that he has never tried it.

In the numerous publications on serpiginous ulcer since that time I could not find any other reference to this procedure. What I cannot find surprising is the serious objections quoted against it. *Ubi pus, ibi evacua*, says the old rule, and we act plainly contrarily. Every further treatment, even the control of the ulcer is made impossible by the covering, and—if only temporarily—we deprive the eye of its remaining small vision, creating at the same time a disadvantageous situation from the cosmetic point of view.

We can set against all these drawbacks one advantage, the saving of an eye, or rather, the saving of vision, that would have been lost by any other treatment. Of course it would outdo all objections, if this could be proved.

There are only two particulars that can be made subjects of enquiry; the visual acuity before and after treatment, and the duration of medical attendance, expressed in the days of hospitalisation.

The total hooding is superior to our own medical treatment. Further comparisons cannot be made on the simple ground that in the whole ophthalmological literature there do not exist records or statistics on serpiginous ulcer comparable to ours.

Our medical (conservative) treatment is the well known general treatment of serpiginous ulcer, always adapted to the case. It consists of heteroprotein injections, administration of sulphonamides, instillation of zinc sulphate, optochin, silver compounds, atropine, and the well known treatment of Eperon, *i.e.*, painting the ulcer and its advancing margins with 20 per cent. zinc sulphate solution. An infected lacrimal sac is removed. For hypopyon, paracentesis of the cornea is done. Of course we used largely all propositions available in our 30 years of practice, *i.e.*, various forms of cauteries, iontophoresis, trepanation of Sonderrmann, chemotherapeutics as rivanol, tryptoflavin, vetol, etc., without any convincing success.

As we have to-date 56 cases treated by full conjunctival hooding, in the following tables we compare these with twice 56 cases of the preceding period treated conservatively in the described manner. The basis of comparison is visual acuity and hospitalisation.



TABLE I

Fifty-six cases of serpiginous ulcer treated conservatively during the period 1935, 6 April—1938, 4 April.

Number	V at beginning	V at end	Days of treatment
1	0	0	15
2	0.1	0.1	10
3	0.1	0	25
4	12	20	8
5	0.1	0.1	7
6	0.1	0.1	24
7	2	2	10
8	0	0	24
9	0.1	0.1	9
10	1	1	11
11	30	30	10
12	12	12	7
13	0.1	0.1	15
14	20	20	8
15	0.1	10	8
16	0.1	0.1	15
17	6	25	19
18	1	15	16
19	0.2	0.2	17
20	0.1	40	7
21	0.1	6	7
22	0.1	0.1	15
23	0	0	13
24	0.1	0	32
25	0.2	0.1	6
26	1	0	8
27	6	15	4
28	0	0	20
29	0.1	0	20
30	0.1	0.2	23
31	0.2	4	7
32	0.1	0.2	11
33	0	0	27
34	0.1	0	22
35	0.1	1	10
36	1	1	7
37	3	12	10
38	6	12	12
39	15	15	9
40	2	10	5
41	0.1	0.2	9
42	0.1	0.1	11
43	0.1	0.1	14
44	0.2	20	10
45	0.1	0.1	19
46	20	25	12
47	6	1	18
48	4	10	10
49	1	15	9
50	3	15	12
51	5	8	5
52	3	6	16
53	2	5	8
54	0.1	3	6
55	20	40	87
56	0.1	0.1	24

TABLE II-

Fifty-six cases of serpiginous ulcer treated conservatively during the period 1938, 6 April—1943, 10 August.

Number	V at beginning	V at end	Days of treatment
1	0.1	8	22
2	3	15	48
3	0	0	10
4	1	15	4
5	1	2	17
6	0	0	29
7	0.1	0.1	28
8	0.1	0	23
9	0.1	0	27
10	0.1	0.1	12
11	0.2	12	8
12	0.2	15	7
13	0.1	0.1	27
14	1	10	9
15	0.1	0.1	27
16	6	8	6
17	0.2	2	19
18	0.1	1	27
19	0.1	0.1	7
20	2	4	10
21	0.1	0.1	22
22	0.1	0.1	21
23	0.1	1	9
24	0.1	15	5
25	0.1	0.1	18
26	1	1	6
27	0.1	2	6
28	1	1	13
29	0.1	0.1	11
30	6	6	6
31	0.1	0.1	11
32	0.1	0.1	23
33	0.1	0.1	28
34	0.1	0.1	10
35	0.1	5	8
36	0.1	0.1	12
37	0.2	25	11
38	0.2	0.1	18
39	0.2	6	6
40	0.1	8	10
41	0.1	12	11
42	15	15	3
43	0	0	27
44	0	0	33
45	0.1	0.1	8
46	15	15	11
47	0	0	17
48	1	1	10
49	0.1	0.1	17
50	1	1	11
51	2	2	5
52	0.1	0.1	11
53	0.1	6	6
54	0.2	6	7
55	3	12	9
56	0.1	0.1	11

TABLE III

Fifty-six cases treated by full conjunctival hooding of the cornea during the period 1940, 4 August—1943, 30 August.

Number	V. at beginning	V. at end	Days of treatment
1	0.1	2	5
2	0.1	0.1	6
3	3	20	4
4	0.1	12	7
5	0	0.5	4
6	0.1	1	6
7	0	15	4
8	0	3	5
9	0.1	0.1	5
10	0.5	25	5
11	0.1	6	5
12	0.1	8	6
13	0	6	7
14	0	0.2	8
15	0.1	8	6
16	0	8	5
17	0	0.1	5
18	0.1	0.1	4
19	2	2	6
20	0	0	7
21	0.1	10	5
22	0	2	4
23	0.1	15	6
24	3	6	5
25	2	4	6
26	4	8	5
27	0.1	3	6
28	0	0.1	5
29	0.1	0.1	7
30	1	2	5
31	0.1	10	6
32	0	15	5
33	0	0	13
34	0.1	6	6
35	0.2	3	5
36	0.1	0.1	6
37	2	25	4
38	0	0	6
39	1	30	7
40	0.1	10	5
41	0.2	8	9
42	0.1	0.1	5
43	0	6	7
44	0.1	12	5
45	3	20	6
46	0.1	1	6
47	0.2	12	7
48	1	20	5
49	0.1	2	4
50	0	3	8
51	0.1	0.2	5
52	3	3	5
53	0.2	4	7
54	1	25	5
55	0.1	4	6
56	0.1	15	5

**R. MILLAURO,**

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To the reading of the tables it has to be mentioned, the visual acuity is recorded in oxyoptries of Blaskovics, as it renders the statistical and comparative discussion of this value very easy. For the rest it is easy to turn from oxyoptry to the current expression of d/D: one has only to make a division by 60, e.g., 3 oxyoptries =  $3/60$ ;  $60/0 = 60/60 = 6/6$ . (The sign of oxyoptry is /o).

Lack of light perception is recorded by 0; light perception is similarly recorded by 0, as  $1/\infty = 0$ , and its practical value is 0 too; hand-movement is recorded by 0, 1/o; counting fingers before the eye 0, 2/o. (It is to be born in mind, this 0, 1 and 0, 2 does not mean one tenth vision, but one tenth oxyoptries).

We find the following facts by simple calculation in the tables.

The 56 cases of Table I sum up to 147, 1/o of visual acuity at the beginning of the treatment; finally round 400/o. Out of every 100/o there became 270.

In the second table this sum total is only 38,9 at the beginning; finally it has grown up to 233,9/o. From every 100/o became 600.

The average of the added two tables says that by conservative treatment we could raise every 100 oxyoptries to 435.

In the third table we could not start with the visual acuity on admission, as we tried generally first the conservative treatment, and operation was only proposed in a progressive case (except serious cases with very low sight at the beginning of the treatment). Hence the second row shows the vision before the intervention. The sum total is only 29,7 /o, that was raised at last to 411,7 /o; in per cent. this would say that every 100 /o became the relatively enormous sum of 1386,2 /o.

But there is arising again a difficulty in not allowing the values to be compared directly. The final visual acuities of Table I and II are recorded on discharge from the clinic, while those of Table III 6-8 months later, after having removed the covering from the cornea. It is very probable, that after the lapse of half a year the vision of the first and second groups improved appreciably also. As we do not work with exact values, and we intend only to avoid a generally erroneous conclusion, we try to eliminate this difficulty by presuming a further improvement of 100 per cent. in the first and second tables and only of 10 per cent. in the hooded cases.

So in conclusion we might state we could augment 100 visual units to 870 by conservative treatment, and to 1,524 units by the total hooding; hence the superiority of the latter seems to be well proved.

There are still some further comparable points regarding vision, e.g., the number of cases improved, worse, and unchanged.

TABLE IV

	Improved	Worse	Unchanged
In Table I	27	7	22
In Table II	26	4	26
In Table III	45	1	10

Further we can pick out the cases when qualitative vision recovered as far as quantitative, that means light perception became again at least finger-counting.

TABLE V

In Table I	...	...	...	...	0
In Table II	...	...	...	...	0
In Table III	...	...	...	...	12

The contrary is similarly instructive, namely, how often qualitative sight turned into quantitative or less; that is, how often the sight has been lost.

TABLE VI

In Table I	...	...	...	...	5
In Table II	...	...	...	...	3
In Table III	...	...	...	...	0

From Table V we could deduce as a rule, that whenever a patient has a vision of not more than 1/o, it is only the total hooding that promises still some small serviceable sight at all.

Table VI is instructive too; it seems to show that the hooding secures us against full visual loss whenever the operation was not made too late. If panophthalmitis is present, restoration of the sight naturally cannot be hoped for any more.

The duration of the hospitalization is much in favour of the hooding. The conservative treatment required averages 14 days, the hooding on the other hand only 6 days. And in these 6 are also included the cases with extirpation of the lacrimal sac, sometimes with inevitable suppuration lengthening the treatment to 8-9 days. Eliminating these cases there remain only 4 days. To these have to be added the 3 days at a later date when the patient returns for removal of the hood.

But these data convincing as they may be, it is the clinical observation that remains conclusive for the surgeon. Pain, lacrimation, irritation, oedema all disappear a few hours after the operation, showing the instantaneous effect of our intervention. The wound of the conjunctiva heals shortly, and the patient leaves hospital though not seeing, yet with the feeling of being healed.

And what I believe to be the most important point in the whole proceeding, the surgeon himself no longer has that annoying feeling of observing a serpiginous ulcer progressing inevitably from day to day under his care.

The time of re-opening has to be set at least 6 months after the operation. Although the healing process begins at the moment of the covering, the pneumococci remain still alive for a time, probably with gradually decreasing virulence. Would we re-open the hooding,

say 2 weeks later, the ulcer would inflame again, and we would be compelled to cover the cornea again, as has happened. Even 2-3 months later we have seen a weak relapse with a small-hypopyon for a few days. As far as our observations go, the interval of at least 6 months has to be kept. It is surprising, how willingly our patients wait, till the set term is over.

The re-opening is a simple procedure. We lift the conjunctiva somewhere on the cornea, make a hole in it through which we introduce the scissors and cut away the flap all around inside the limbus. The parts grown together are detached as a pseudopterygium by iris-spatula and keratome. One has to take care not to leave a thin capsular layer on the cornea. The eye is dressed for 1 to 3 days.

Encouraged by the satisfactory results, recently we have begun to extend considerably the sphere of application of the total hooding, i.e., to all acute and chronic keratitic processes unhealed or not healing well, such as ulcerated and degenerated pannus, ulcus destruens, herpes corneae, kerato-mycosis, neuromyolytic keratitis. Once we applied it to an enormous exophthalmos in Graves' disease with excellent result.

Thus the total conjunctival hooding of the cornea became at my clinic an increasingly employed proceeding for keratitic processes and it is my firm conviction that we can save eyes by it, that would be otherwise inevitably lost.

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## LOCAL SULPHONAMIDE THERAPY OF DENDRITIC ULCER\*

BY

H. L. HUGHES

LONDON

IN the early days of sulphonamide therapy Kleefeld (1938) recorded favourable results from the general administration of the drug in six cases of dendritic ulceration and in twenty cases of corneal herpes. Schmid and Saubermann (1942) likewise obtained satisfactory results in five out of twenty-one cases of herpes corneae. Most



observers, however, have had a less favourable experience but Sorsby (1944) has drawn attention to the value of local therapy in dendritic ulcer. He reported unexpectedly encouraging results from the intensive use of local sulphonamide therapy in sixteen consecutive cases. Improvement was generally rapid and most eyes, though not fully cured, were symptomless within ten to fourteen days.

### A Series of 16 cases

*Clinical features.*—Local therapy was employed in a series of sixteen consecutive cases seen during January–April, 1947. The clinical details are set forth in Table I. It will be noted that twelve cases out of sixteen responded to treatment, and that in six of these twelve cases, the response was particularly good. The cases showing a good response (Nos. 1–6 in Table I) showed the following features:—

(1) Morphologically the ulcers were all small, typical dendritic figures occupying an area about  $1 \times 1\frac{1}{2}$  mm. in an otherwise healthy looking cornea.

(2) Sensation was diminished in three cases, normal in two, and appeared relatively increased in one.

(3) The duration of the symptoms before treatment varied from 7–21 days, and all cases were clinically cured within 8 days.

The six cases that gave a fair response, varied from the first group in that:

(1) The ulcers were more extensive. In two cases the dendritic figure appeared upon a cornea the seat of pre-existing ulceration of long duration.

(2) Sensation was diminished in all cases, and in three remained absent throughout treatment. In the remaining three it was very slow in returning.

(3) The duration of the symptoms before treatment varied from 2–10 days. The total duration of treatment was from 14–28 days, but the cases were all asymptomatic in 6–13 days.

The last group of four cases included one which was identical clinically with those of Group 1, whilst three had much more marked corneal involvement, varying from multiple punctate opacities to generalised oedema of the cornea. Case No. 16 was associated with German measles and showed a severe lesion.

### Mode of Treatment

Six per cent. albucid ointment (Schering) was instilled thrice daily, and the entire corneal surface painted once daily with 30% albucid solution. This necessitated a daily attendance.

As may be seen from Table I, the subsidence of acute symptoms was rapid in successful cases, and the eye rapidly became white.

TABLE I: Clinical features in sixteen cases of dendritic ulcer treated by sulphonamides locally.

No.	Sex	Age	History of previous attack	Duration in days before treatment	History of preceding febrile disturbance	Presence of febrile disturbance when first seen	Extent of ulcer	Rest of cornea	Corneal sensation	Number of days to control acute symptoms	Total number days treated	Response to local sulphonamide therapy
1	F	58	None	21	No	None	Small	Two punctate opacities Clear	Diminished	3	8	Good
2	F	29	None	10	Yes	None	Small	Clear	Diminished	2	8	Good
3	M	27	None	10	Yes	None	Small	Clear	Increased	3	3	Good
4	M	35	None	4	Yes	None	Small	Two punctate opacities Clear	Normal	3	3	Good
5	M	43	None	4	Yes	None	Small	Clear	Normal	6	6	Good
6	M	53	None	7	Yes	None	Small	Clear	Diminished	6	6	Good
7	F	34	Yes (3)	2	Yes	None	Small	Old scar	Diminished	6	27	Fair
8	F	39	None	11	None	None	Small	Clear	Diminished	Not definite	48	Fair
9	M	58	None	10	Yes	None	Moderate	Clear	Diminished	Developed atropine irritation	18	Fair
10	M	29	None	6	Yes	Yes (Associated Herpes Labialis)	Large	Clear	Diminished	7	21	Fair
11	F	8	Yes (4)	6	None	None	Large	Old vascularised scar Clear	Diminished	13	13	Fair
12	F	40	None	7	No	None	Moderate	Clear	Diminished	7	28	Fair
13	M	58	None	14	None	None	Small	Clear	Diminished	Not definite	Still under treatment after 60 days	Poor
14	M	49	None	10	Yes	None	Moderate	Multiple punctate opacities	Diminished	Not definite	Still under treatment after 70 days	Poor
15	F	43	Yes	7	Yes	None	Large	Old vascularised scar	None	Not definite	Still under treatment after 52 days	Poor
16	M	84	Yes	8	Yes	Yes (German measles)	Large	Oedematous	Diminished	Not controlled	Changed to iodine after 11 days	Poor

Routine guttae atropine 1% daily, and a pad and bandage was used in all cases. The cases that were not controlled by local sulphonamide were treated by iodine cauterisation. The response to iodine therapy in Case No. 16 (associated with German measles) was dramatic, after 11 days treatment without any obvious response to albucid.

*Prognosis.*—Clinically the cases fall into three categories. In the first the lesion is superficial and does not appear to penetrate beyond Bowman's membrane. On painting such a case the characteristic figure is removed and a diffuse stain is left. This healed rapidly under the local therapy.

In the second group the lesion goes deeper into the substantia propria, and the dendriform figure can still be made out after removal of all loose epithelium. These cases took longer, but healed without severe scarring, though some scarring was always present.

In the third type there was diffuse opacity in the substantia propria. Whether arising *de novo* or superimposed upon an old corneal lesion these cases proved more difficult to treat.

The age of the patient did not appear to influence the type, activity, or response to treatment.

Corneal sensation rather than size of the ulcer seems to afford the best guide to the progress of the lesion. Cases with marked depression of sensation were slow to heal, and healing progressed parallel with the return of sensation. Cases with little or no loss of sensation when first seen responded rapidly.

### Theoretical Considerations

Dendritic ulcer is regarded as a herpes virus infection. Theoretically it should not respond to sulphonamide therapy. As Sorsby points out the good results recorded by him (and confirmed in the present study), raise the question whether the current views on the aetiology of dendritic ulcer are valid. It is, of course, also possible that the high concentration reached by local treatment is effective against the virus.

My thanks are due to Professor Arnold Sorsby for the constant help and encouragement he has given me, and to the members of the staff of the Royal Eye Hospital who have helped me to obtain the material and assisted me in every possible way.

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DATA ON THE OCCURRENCE OF CALCIFICATION  
IN THE EYE TISSUES\*†

BY

MAGDA RADNÓT

BUDAPEST

ONE of the most widely known degenerations of the cornea occurs in the form of zonular opacity, which can be observed in the region of the palpebral aperture in the form of a band narrowing towards the centre from the limbus, leaving here a narrow strip of the cornea free. The anatomical basis of this clinical picture is a calcified degeneration of the layers under the epithelium of the cornea. The text-books distinguish two or three forms of zonular opacity. One is pathologically quite a different deformation, occurs as an occupational injury, principally to hat-makers, and is caused by the deposit of rabbit hairs in the cornea. The other two forms are the so-called primary and secondary ribbon-type degeneration, the difference between them being that the primary occurs in eyes otherwise healthy, the secondary in damaged eyes, usually those blinded by uveitis. Merz-Wigandt has warned that this distinction is not justifiable, as it is possible that the primary also occurs in previously injured eyes but that it cannot be demonstrated clinically.

As we have intimated, the essential change is a lime deposit. This, according to Leber, develops the clinical form of zonular opacity, because the greatest degree of evaporation is in the region where the eye opens and the calcium precipitates here from the greater calcium-containing liquid coming into the cornea. This explanation is not universally accepted, but, as Hippel remarked, no one knows a better one. Imre's observation is very interesting, to the effect that in one case of transplantation of the cornea because of zonular opacity, a change similar to zonular opacity showed itself in the transplanted disc too.

In the following we deal with cases of the so-called ribbon-type degeneration, seeking what changes we find in the other tissues of the eye, first of all whether we find calcareous deposits elsewhere too.

Calcification also occurs in the cornea secondarily in leucoma and, very seldom, in the form of primary calcareous deposit. In Axenfeld's well-known primary case and in one case of Imre's the cause of the calcareous deposit could not be cleared up. These changes do not come within the limits of the present investigations, no more do those cases when lime is deposited in the cornea in connection

\*Publication of the Ophthalmological Clinic No. II Budapest (Director, Professor Tibor Nónay).

† Received for publication, June 9, 1947.

with lime injury (Lisch), nor the lime deposit occurring in osteomalacia (Spärlang).

At a meeting of the Hungarian Ophthalmological Society on October 5, 1941, we presented 6 cases, 4 of which were zonular opacity, the other 2 consisting of lime in the cornea in the form of irregular deposits. In all 6 cases we found lime deposits in other tissues of the eye-ball also. Since then we have, with special attention to this viewpoint, investigated the eye-balls in the corneas of which we saw calcareous degeneration. In the following, on the



FIG. 1.

Calcareous deposits in Bowman's membrane and beneath it.



FIG. 2.

Bowman's membrane absent.

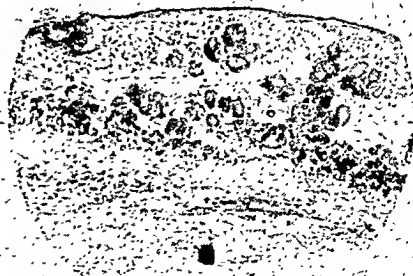


FIG. 3.

Calcareous scar tissue under the epithelium

basis of 12 cases, we describe the occurrence of lime in the eye tissues. In ten of them lime was deposited in the cornea as zonular opacity, in the other two in an irregular form.

Walsh mentions similar degeneration of the conjunctiva in a case of zonular opacity arising after iridocyclitis, and under a figure of Hippel's we read that "Bandförmige Hornhauttrübung . . . Auge mit ungewöhnlich starker Verkalkung in der Retina."

In a case of zonular opacity we found calcareous deposit in the region of Bowman's membrane and in the form of discs in layers under it (Fig. 1). In most cases hyaline granules could also be found

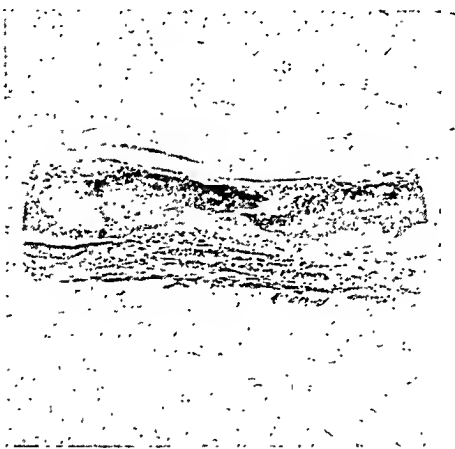


FIG. 4.

Bone lamellae in the choroid.

beside the calcareous lamellae. In the more advanced cases the calcification is very extensive. Bowman's membrane is lacking, and scar-tissue develops under the epithelium (Figs. 2 and 3). Lime can most frequently be found in the choroid also in these cases, that is, in bone lamellae. Besides the changes in the cornea to be seen in Figs. 2 and 3, we found bone lamellae in the choroid (Fig. 4). Much more extensive bone formation is to be seen in the case shown in Fig. 5, where, in addition, a calcareous degeneration is also to be observed in the subluxated lens. Somewhat more rare is the deposit of lime in the degenerate retina, or in chorio-retinitis scars (Fig. 6).

If the lime deposit is extensive the changes will be perceptible with X-rays. In Fig. 7 can be seen a bone cup in place of the choroid and the calcified lens; the same bone cup dissected is shown in Fig. 8. In Fig. 9 is a case of greater calcification of the lens, with a smaller amount of lime observable in the choroid. The X-ray photographs were taken by Dr. Luzsa.

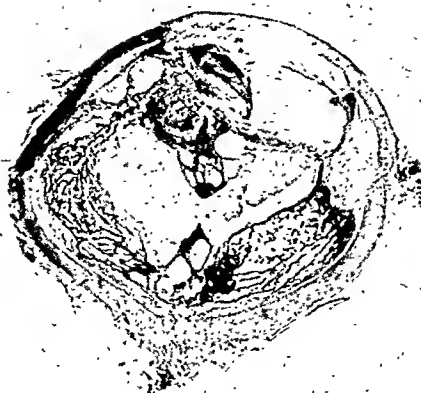


FIG. 5.

Half eye showing extensive bone formation and calcareous degeneration.



FIG. 6.

Lime deposit in degenerate retina.



FIG. 7.

Choroid replaced by a bone cup and lens calcified. X-ray photograph.



FIG. 8.

Bone cup dissected out of eye.

FIG. 9.

Lens more calcified than in Fig. 7, choroid less calcified. X-ray photograph.



FIG. 10.

Bone lamellae in chorio-retinal scar.



FIG. 11.

Secondary glaucoma, accompanying chronic uveitis.



Cataracta calcarea, according to Szily's observations, generally occurs in connection with uveitis and accompanies lime deposit in the choroid.

In exceptional cases the bone formation can extend into the tissues of the cornea, as in Zwiäuer's case.

In chorio-retinal scars not only simple lime deposits but also the formation of bone lamellae is possible (Fig. 10). Zonular opacity is to be observed in most cases in atrophied eyes, and in Fig. 11



FIG. 12.

Calcareous deposits in lamina vitrea warts.

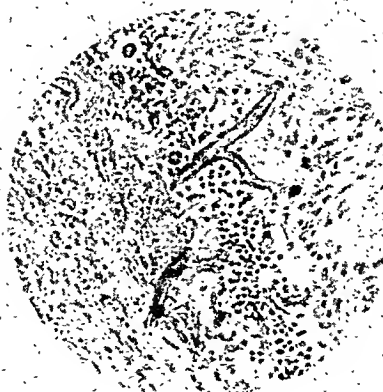


FIG. 13.

Calcareous deposits in detached retina of same case.



FIG. 14.

Calcareous lamellae in optic nerve.

there can be seen in a case of ours the secondary glaucoma accompanying chronic uveitis which led to enucleation (Fig. 11).

In atrophied eyes lamina vitrea warts are very often to be seen, but only very rarely is a lime deposit found in them, as in Fig. 12. In the same case we saw calcareous deposition in the layer of the retina which was wholly detached and gathered into wrinkles in the anterior part of the vitreous body (Fig. 13). In the wall of the bigger obliterated vessels, or in the hyaline centres which are to be found in their place, the lime deposit is principally to be seen in the detached retina.

It does not strictly belong to our subject but because of its rarity we present Fig. 14, where we find lime lamellae in the optic nerve in an eye blinded by a malignant exophthalmos. The corpora amylacea occurring in the covering of the optic nerve usually contain more or less lime.

On the basis of our investigations, therefore, we see that when lime is deposited in the cornea in zonular opacity or in eyes injured in some other way, a lime deposit is also to be found in the other tissues of the eye-ball.

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## TREATMENT OF PERFORATED CORNEAL ULCER BY AUTOPLASTIC SCLERAL TRANSPLANTATION\*

BY

SVEN LARSSON

LUND

THE method generally used in trying to close a persistent corneal defect is either that of covering it with conjunctiva which has been detached in some way, or that of corneal grafting. In cases where the defect lies outside the optic zone, and optical considerations do not arise, a conjunctivoplasty would seem to be the current method, and is in fact successful in most cases. If, however, transparency is aimed at, transplantation of cornea has lately been used with ever increasing frequency.

In the literature at my disposal I have found no account of attempts to close a persistent corneal defect or fistula by transplantation of sclera taken from the patient's own eye. Such an attempt will be described here.

The patient, a seven year old girl, M.E. 977/45, had previously been healthy. In July, 1945, a left-sided exophthalmus occurred, and as the X-ray examination showed a decalcification of the left wing of the sphenoid the doctor in charge of the case suspected a tumour with intracranial extension. The patient was, therefore, sent to the neuro-surgical clinic of the Serafimer Hospital in Stockholm. A copy of the patient's case history has been placed at our disposal.

The following data were recorded on admittance on September 14, 1945:

Vision R.E. 5/5, L.E. 5/10.

The right eye showed no symptoms of abnormality.

The left eye protruded considerably. Hertel's exophthalmometer showed 13 mm. for the right eye and 19 mm. for the left eye, i.e., an exophthalmos of 6 mm.

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† From the Ophthalmic Clinic of the University of Lund, Sweden. Chief: Professor Sven Larsson.

Papilloedema with about 4D. protrusion in the left fundus.

The X-ray showed a decalcification in the rear and lateral wall of the left orbit, which was probably due to atrophy caused by pressure. For this reason an orbital tumour was assumed.

The patient was operated on September 21 (Prof. Olivecrona), and a cavernous angioma was removed after unroofing the orbit. The histopathological examination revealed a cavernous haemangioma. On the following day the patient became unconscious and had Jacksonian fits. As a haematoma was suspected, the bone flap was lifted and a medium-sized extradural haematoma was removed.

Ptosis, protrusion of the left eye, and failure of the eyelid to cover the lower part of the cornea were recorded during the post-operative course. An ulcer appeared in the lower part of the cornea. In other respects progress was favourable, and the patient was discharged on October 5, 1945, to be treated further by an eye-specialist in her home region.

The patient's lagophthalmic keratitis did not, however, heal. A descemetocoele appeared, which was cauterized and covered by a conjunctival flap. The operation, repeated no less than three times, was unsuccessful. The wound grew larger, nutritive impairment was suspected, and on December 28, 1945, the patient was sent to the ophthalmological clinic at Lund.

We recorded the following data:

Vision R.E.=1 ( $\pm 0$ ). L.E.=0.2; no improvement with glasses. Right eye normal.

Left eye: A slight ptosis. The eye turned slightly downwards and outwards indicating paresis of the IIIrd nerve. The eye did not protrude. Intense injection (as a result of all the earlier operative measures). In the lower part of the cornea a few mm. from the limbus, a descemetocoele somewhat larger than the head of a pin, was discovered and close to this the cornea was a muddy grey. The eye was otherwise free from irritation, and there were no signs of iritis. Ophthalmoscopically the eye was normal. Reduced sensibility of the cornea could not definitely be established.

The patient was operated on on January 12, 1946. A conjunctival flap was dissected downwards, during which process the bulbous became rather soft owing to leakage from the corneal defect. This, however, only slightly impeded the operation. The sclera near to the insertion of the external rectus was exposed and a scleral disc was punched out near the lower border of the rectus tendon by means of a 2.5 mm. trephine. This was lifted up without damaging the choroid. The corneal

hole was manipulated in order to obtain a circular defect, a good 2 mm. in diameter and as clean cut as possible. The scleral disc was then easily fitted into the hole, whereupon the conjunctival flap was drawn over the graft and sutured. A double bandage was applied.

The post-operative course was without complications: no irritation at all; the anterior chamber was soon regenerated.

January 26, 1946; no irritation. The conjunctival flap still remained and covered a large part of the cornea. Through the flap the white scleral disc could be seen in position. No fistula. The patient was discharged.

March 7, 1946; no irritation. Through the translucent conjunctival flap, which now covered only the lower part of the cornea, the transplanted white scleral disc was still seen to fill up the former defect. The corneal surface was completely smooth. The pupil was round, but nasally and downwardly the iris had probably healed a little to the inner side of the cornea. No fistula. Tension, 22 mm. Hg. Vision = 0.5 (+1.0 D.Sph. +2.0 D.Cyl. 180°). A slight ptosis still persisted, together with a slight deviation, downwards and outwards, of the bulbus.

### Discussion

The corneal affection communicated here was undoubtedly a lagophthalmic keratitis, since it arose in connection with a post-operative inability to close the eye. It is, of course, impossible to decide whether impaired circulatory and nutritive conditions—caused by the operative measures—contributed towards the genesis of the corneal injury. There were, however, no grounds for assuming neuromyopathic keratitis.

The ulcerative corneal process advanced, and as no less than four attempts had been made by others to cover the wound and cause it to heal by means of common cauterization and conjunctivoplasty, I thought a plastic operation of a different kind was indicated. Because of the comparatively peripheral site of the ulcer, the graft did not need to be transparent and therefore optical considerations could be disregarded. As a result of the wide experience of scleral trephining I had gained from my earlier operations for detachment of the retina, I was attracted by the idea of trying to close the corneal defect by means of a scleral disc punched out of the same eye. The operation here described in detail did not present any difficulties, and its course was entirely favourable. The method might well be remembered in cases of corneal ulcer or fistula where other more simple methods do not lead to the desired result.

### Summary

In connection with an operation for retrobulbar haemangioma, a seven year old girl got a lagophthalmic corneal ulcer which developed into a descemetocoele. Four attempts elsewhere to close the ulcer with a conjunctival flap did not lead to the desired result. The wound got larger, and there was danger of perforation. A scleral disc was punched out of the same eye and transplanted into the wound, after the edges of the latter had been excised. The graft was covered with conjunctiva. The result was good: the transplant fitted in comfortably, the ulcer closed, and vision was comparatively good.

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### ANNOTATION

Sir Charles Sherrington, O.M., F.R.S.

Sir Charles Sherrington celebrated his ninetieth birthday on November 27 last. When we remember that some of his experiments on ocular movements and visual phenomena provided the most crucial evidence for great discoveries, it is a fitting and altogether congenial duty that ophthalmologists should add their quota to the paean of praise. His investigations of muscle spindles and the afferent nerve fibres from extrinsic eye muscles initiated his study of proprioceptive nerves; and this in turn led to the discovery of the physiological substrata of posture as fully elaborated by him and by his pupil Magnus. It was, too, from conjugate movements of the eye, induced by stimulation of the frontal ocular motor area, that he obtained some of the strongest evidence of the inhibition of antagonistic muscles, thus again opening up a vast new conception of active processes other than mere excitation occurring in motor phenomena.

Pure mathematicians are always anxious to obtain the neatest and most "beautiful" solution of a problem. Sherrington's experiments on binocular vision belong to this category. They prove the absence of simple summation of the responses from the two eyes; but the philosophical meaning goes far beyond so simple a fact. They show that "for each eye the sensorium carries elaboration of sub-perceptual and perceptual vision to a considerable pitch of mental completeness without marked collaboration between the visual processes of the two eyes."

Of even more far-reaching importance were his experiments on cortical motor areas, which broke down the jejune idea of mere anatomical representation of muscular action in the cortex cerebri, and so "first within the brain discerned the meaning of its ordered

ways, and man of his own nature learned to thread the labyrinthine maze" (W. Russell Brain\*). At the hands of his pupil Granit, the processes of excitation, facilitation, inhibition, and so on, demonstrated by Sherrington in the spinal cord, have been shown to regulate impulses in the retina and optic nerve. This isolated mass of brain, with its equally isolated intra-cerebral pathway, the optic nerve and optic tract, are thus shown to be a specially favourable locus for future experimentation. And so Sherrington has been led on from "The Integrative Action of the Nervous System" to the profound philosophical conception of the relationship of body and mind contained in "Man on his Nature."

Great then are Sherrington's scientific claims to greatness—claims which, as has been pointed out, justify comparison with Harvey, marking an epoch in biology. And those who have had the privilege of knowing Sherrington, the man, realize that his meticulous scientific integrity is combined with an endearing kindliness, and a modesty without which no man is truly great.

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## FACULTY OF OPHTHALMOLOGISTS

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### Report of Council Meeting on October 10

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THE Honorary Secretary drew attention to the very brief report of the Faculty's activities that had appeared in the *British Medical Journal* and the *Lancet*, as compared with that in the *British Journal of Ophthalmology*. It was agreed that the Honorary Secretary should ask the *British Medical Journal* and the *Lancet* to realise that the report was already cut to a minimum and to ask for it to be printed as submitted.

The Faculty had asked the British Medical Association to confirm the statement that compensation would be given for consultant practices and a reply has been received that the buying and selling of consultant practices in general was not prohibited by the National Health Service Act and for this reason the compensation provisions of the Act did not extend beyond the cases of general practitioners whose names were entered "on the appointed day on any list of medical practitioners undertaking to provide general medical services."

It was reported that the Medico-Political Standing Committee had submitted a Memorandum to the Evidence Committee, sitting under the Chairmanship of the President of the Royal College of Surgeons, on the remuneration of consultants and specialists.

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\* *Lancet*, November, 22, 1947.

With reference to orthoptic matters, it was reported that the Local Authorities would not accept a salary scale for orthoptists approved by the Faculty or any other professional body, but asked for a properly negotiated scale between employers and employees. It was, however, noted that the Joint Negotiating Committee's salary scale was acceptable to the Faculty and therefore it was decided to take no further action.

The question of standards of vision for orthoptic students was reviewed and the following resolution adopted :—

“ Visual acuity should be 6/9 corrected in each eye, with full binocular vision, It is undesirable to have more than 7 D. refractive error in any meridian, but such cases could be accepted at the discretion of an ophthalmic surgeon.”

A letter had been received from the Ministry of Education requesting the Faculty's opinion on plastic lenses for school children. It was decided that, in view of the present state of development of plastic lenses, particularly their softness and their liability to scratch, the Council did not consider that they were a practical proposition for universal use at the moment.

Following correspondence with a Joint Committee set up by the B.M.A. and the Pharmaceutical Society to compile a National Formulary suitable for use in connection with the National Health Service, the Faculty nominated three representatives to serve on a Sub-Committee to consider the draft section of the Formulary concerning ophthalmology.

The attention of the Faculty Council was called to the fees for School Ophthalmic Work from two sources. In view of the fact that the scale of fees for all Local Authority work had been negotiated by the B.M.A. for all consultant and specialist work, it was decided that no further action could be taken at the moment.

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## BOOK NOTICE

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**Contact Lenses.** By THEO E. OBRIG. Second edition. 546 pp., 180 illustrations. Published by The Chiltern Co., Philadelphia, Pa. 1947.

This edition is larger than its predecessor. It gives a general account of the history and principles of contact lens work and a detailed description of the fitting methods practiced by the author. The indications for the use of contact lenses are fully described, applied anatomy, physiology, and optics are discussed, and a short chapter is devoted to the properties of plastics. The detailed description of technique applies to the author's All Plastic moulded



contact lens. The eye is moulded in mouldite, and a semi-finished lens is produced to correspond with this mould. This is modified by grinding to give an exact fit. The formation of Sattler's veil and the probable causes are described in detail, but no mention is made of fenestration as a possible solution of this problem. This book contains much that is of interest to all ophthalmologists, and much that is of value to all students of contact lenses.

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## CORRESPONDENCE

### CONTACT GLASSES AND VEILING

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—If the cornea and adjacent conjunctiva is examined with the slit-lamp immediately after a contact lens is removed when veiling is well established it will be seen that this condition is an oedema of both the cornea and conjunctiva which are not supported by (that is, are not in contact with) the lens. If a contact lens containing paraffin wax melting at body temperature is inserted and left in for an hour or so in a case which easily develops veiling, and the wax is chilled to set it before removing the lens, a plaster model of the eye may easily be made. Such a cast shows a heaped up frill of conjunctiva surrounding the cornea and tending to fill the space between the eye and the lens, where a pool of fluorescein would appear when fitting. If a channel, say  $\frac{1}{2}$  mm. wide and  $\frac{1}{4}$  mm. deep, is cut leading away from the corneal segment of the contact lens and on the inner surface and the lens worn until veiling occurs, when the lens is removed the eye will show an oedematous frill of conjunctiva around the limbus and also that the conjunctiva is herniated into the channel. This raised conjunctiva is easily seen with the naked eye. It is generally recognised that a lens under which veiling has developed "sticks" and is difficult to remove and it can also be shown that at this time the space between the lens and the cornea is less than it was when the lens was inserted.

These facts seem compatible only with the supposition that veiling is due to oedema of the unsupported eye tissues under a contact lens and is due to direct physical suction. This negative pressure may be developed as follows:—a lens with corneal clearance but with an edge fit, when pressed (by the lids) against the globe creates a positive pressure in the fluid under the lens which easily escapes at the lens edge. When the pressure is released, however, the lens edge acts as a valve and neither air nor



PROFESSOR HENNING RØNNE

## OBITUARY

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### PROFESSOR HENNING RØNNE

Dr. E. Godtfredsen writes:—

Professor Henning Rønne died on September 28, after having been seriously ill for more than a year with hemiplegia and aphasia. The death of Professor Rønne is a sad loss to Danish ophthalmology, which he, more than any other, formed and developed after his appointment as Professor of Ophthalmology in Copenhagen in 1931.

Rønne was born on May 25, 1878, and graduated M.B. B.Ch. in 1903. He immediately began to specialize in ophthalmology in different Copenhagen clinics. Among his superiors Bjerrum was the man who became of the greatest importance to him. Rønne's scientific production comprised in the first instance a number of original papers dealing with the visual pathway, investigations into the primary visual centres in the midbrain, and visual field investigations with demonstration of the nasal step in glaucoma simplex. The series of visual pathway papers was introduced in his M.D. thesis in 1910: "Anatomical, Pathological, and Clinical Studies on Alcoholic Amblyopia." Immediately before his illness Rønne finished a paper giving a comprehensive account of the Architecture of the Visual Pathway. Rønne's numerous contributions to periodicals show his wide interests and knowledge of such subjects as colour sense, Weber's law, dark vision, squint, orbital inflammations, choroidal sarcoma, syphilitic choroiditis, and dyslexia, to mention only the more important.

Rønne's great interest in the pathological anatomy of the eye manifested itself in the establishment of a central laboratory attached to the Eye Department of the Rigshospital, to which all eyes enucleated in Denmark are sent.

In addition to his great work as university professor and head of the leading eye clinic of Denmark. Rønne had a large private practice. He was widely travelled and was honorary member of various foreign societies, including the Royal Society of Medicine.

Danish ophthalmology is much indebted to Professor Rønne, whose ardent and never abating interest in his profession and ever inspiring eagerness to discuss new problems will remain an unforgettable and stimulating example to us young ophthalmologists who were his pupils.

## OBITUARY

Dr. A. H. H. Sinclair writes:—

It was fortunate that a man of the late Professor Henning Rønne's remarkable ability and enthusiasm in the pursuit of clinical research should have been closely associated during his early years as ophthalmologist with Professor Bjerrum. This indeed was a mutual advantage: in this connection Rønne had the opportunity of which he fully availed himself, to become intimately acquainted with Bjerrum's method and technique. But, in addition by his keen observation of the form, position and density of visual defects found within the area of the field of vision and his great and increasing knowledge of the visual pathways, he soon became able to throw fresh light on the clinical significance of field defects he had graphically demonstrated by the use of Bjerrum's screen test. This method he described as the quantitative method.

In 1911 I paid my first visit to Copenhagen in order to become personally acquainted with Prof. Bjerrum and his already famous junior, Dr. Rønne. On arrival I found that Prof. Bjerrum had just retired from the Chair of Ophthalmology: he was, however, at work in another clinic, where I was much interested to meet him: he expressed to me his pleasure in the interest taken in his work in Britain. At the University clinic I found Dr. Rønne hard at work: I soon realised that he was very fully occupied there. He kindly invited me to his home in the evening, where I was much interested to hear his remarks as he described some of his records and charts of the visual fields: I was delighted to note the humorous enthusiasm with which he told me of fresh projects of research he had in view.

I met Rønne on two subsequent occasions: once in 1927 when he stayed with me in Edinburgh and read a Paper on Optic Neuritis to the Ophthalmological Section of the B.M.A. Meeting, and again on a later visit to Copenhagen when he was Professor of Ophthalmology.

Some years prior to my visit to Copenhagen (in 1911) Rønne had become renowned by his discovery of the 'Nasal step' in the field of vision in glaucoma. Michel in 1874 had described the anatomically arched form of the retinal nerve fibres in the temporal retina, encircling the region of the macula and forming the horizontal raphe extending from the macula to the temporal periphery. The physiological function associated with this anatomical form could not have

been demonstrated and understood unless it had been revealed by a pathological functional failure of conduction in a nerve bundle subjected to injury, in this case pressure at the margin of the optic disc.

Rønne not only recorded graphically the exact form, size and position of the nasal scotoma with its sharp horizontal limitation, (the nasal step), but referred its cause directly to the arched form and position of the temporal retinal nerve bundle. The scotoma forms the counterpart in the nasal field of the functional nerve bundle in the temporal retina.

Investigations of a similar kind were carried on by Rønne in connection with his further study of the visual pathways.

In the wide range of Rønne's activities in research the element which has most permanently impressed ophthalmologists in this country has been the diagnostic value of subjective symptoms as demonstrated by Rønne's use of the quantitative method in his careful scrutiny of the field of vision, and the application of such subjective findings on graphic records to the consideration of their significance in relation to the visual pathways.



## WARNING

*In the note on Welder's Conjunctivitis, Vol. XXXI, p. 774, it was suggested that chlorate of calcium was an error for chloride of calcium. We are informed that so strong a solution of the chloride as 2 per cent. would have dangerous caustic qualities and be unsuitable for use as eyedrops.*

tears can flow in to fill the space which tends to reform under the lens as the eyeball tends to resume its normal shape. A negative pressure is thus created and with each successive lid closure, especially if the lids are tightly squeezed, more fluid is expelled and a greater negative pressure created. This negative pressure may be accommodated in two ways. First by the actual herniation of the conjunctiva which is mobile and secondly by the passage of lymph into the tissue spaces; this oedema is first seen immediately under the epithelium. The system does not impede the centripetal flow of lymph.

It seemed to me, some years ago, that this must be the explanation of veiling—the contact lens acts as a cupping glass—but only recently have I been able to demonstrate the truth of this assumption. It is well known that a badly fitting lens, or one with a suitably drilled hole, will not cause veiling. If instead of these means a channel of suitable dimensions and location is cut on the underside of the contact lens from the lens edge to the pre-corneal space veiling is relieved and bubbles need not be introduced. The channels may be open to the under surface or designed within the body of the material of the lens.

This procedure has proved successful in twelve consecutive cases which I have recently fitted with moulded plastic lenses. I am putting forward this explanation of the condition and the method of dealing with it based upon this explanation, so that others may make use of them. More work will be needed before it is possible to define exactly the technical details as to form, position and number of the channels required. This I hope to make the subject of a formal communication in the future but it seems unjustifiable to withhold an explanation and a method of cure which may be of material assistance to others while the whole problem is being worked out.

Yours sincerely,

FREDERICK RIDLEY.

80, HARLEY STREET,  
LONDON, W.1

November 19, 1947.

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## OBITUARY

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### MacGILLIVRAY of MacGILLIVRAY

MACGILLIVRAY of MacGillivray, after a long and distinguished career as an ophthalmic surgeon in Dundee, died on October 15, 1947 at the age of 82 years. He was ophthalmic surgeon to the Dundee Royal Infirmary for over 30 years, and surgeon to the

Dundee Eye Institution for 45 years. On his retirement from the latter post in 1937 he was presented with a portrait-bust by Benno Schotz, R.S.A., in appreciation of his eminent services. In 1935 he retired from the post of Reader in Ophthalmology at the University of St. Andrews and later received the honorary degree of LL.D. He was for many years eye specialist to the education authorities of Dundee, Angus and Fife. During the 1914-18 war, after long service in the Territorial Army, he acted as consulting ophthalmic surgeon with the rank of major, being awarded the T.D.

Angus MacGillivray after taken an honours medical degree at Aberdeen University, worked under Priestley Smith in Birmingham and was English Secretary at the IXth. International Ophthalmological Congress in Utrecht. In Dundee his work quickly gained for him an outstanding reputation throughout the East of Scotland as well as further afield. He developed unusual skill as an operator, and was a pioneer in cataract extraction under a conjunctival bridge and in the use of retro-bulbar anaesthesia. As a teacher of his subject his clarity of mind and enthusiasm inspired many of his students to take up the study of ophthalmology, and several of them have attained distinction in the speciality.

Born at Abriachan, he was the 28th Chief of the clan MacGillivray, and an enthusiastic of things Celtic and archaeological, having published several books and articles on these subjects. He was Chief of the Dundee Highland Society in 1912. He also took a leading part in many other activities. In 1898 he was Secretary of the Section of Ophthalmology at the Annual Meeting of the B.M.A., and in 1902 Vice-president. In 1924 he was elected President of the Dundee Branch. For 13 years he acted as county controller and director of the Dundee Branch of the British Red Cross Society. Latterly he gave several years of useful service as a member of the Court of St. Andrews University.

MacGillivray of MacGillivray was a man of active mind and vigorous personality, a kindly host and an interesting conversationalist. His passing is greatly deplored by a wide circle of friends and admirers.

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### SELIG HECHT

WE regret to record the death of Professor Selig Hecht, of New York.

Professor H. Hartridge writes:—

Many years ago Banister, Lythgoe and myself were doing some visual acuity measurements at Cambridge, out-of-doors in the sun, when a stranger approached us and stood watching us for a few minutes. I was struck at once by his appearance, because he had an exceptionally fine head and very broad shoulders. He introduced

himself to us: he was Selig Hecht, of Columbia University. We chatted together and soon became firm friends.

During the year that he and his family were in Cambridge I learned many things about Hecht. He was a man of singular energy, initiative and inventiveness. He was also very warm-hearted. His work in the field of vision is well known to all. For no one has done more than he to put the duplicity theory on a sound basis, or to throw light on the factors concerned with the acuity of vision.

In July this year Professor Hecht visited this country again, in order to attend the International Physiological Congress at Oxford and the Conference on Colour Vision at Cambridge. During this visit he stayed a few days at Northwood with my wife and me and we were able to renew the friendship of years gone by. We noticed at once that he was far from well; it was clear that the war years had told on him as they had on us. But none of us suspected how really ill he was.

There is always a tendency for the elderly to think that there is no one to take their place, but this does indeed seem to be the case with regard to Selig Hecht. The physiology of vision has lost a leader at a time when leadership in this subject is very badly needed, indeed. We mourn the loss of a true friend and a very great physiologist.

Sir John Parsons writes:—

The meeting of the International Congress of Physiology at Oxford this year attracted physiologists from all parts of the world. Among them were most of those best known for their researches on the optics, bio-chemistry, and neurology of vision. It was a brilliant inspiration of Wright, Willmer, Stiles, and others to gather them together at Cambridge in the following week for informal discussions on the problems of vision. The meeting was so successful that a volume of the chief communications is being prepared for publication.

Among those present were Hecht, Wald, Granit, and others, and it was a delightful experience to meet or renew acquaintance with them. No one showed greater enthusiasm than Hecht, and no one showed a wiser or shrewder grasp of the bio-chemical problems, to the elucidation of which he has devoted his life's work. (In the *Annual Review of Biochemistry*, Vol. XI, 1942, he has given a brilliant historical review of researches on the chemistry of visual substances, with a complete bibliography). His somewhat dogmatic presentation of arguments was tempered by humour and sweet reasonableness which stripped it of all offence. I think no one was more *persona grata* than he; and it was a profound shock to hear of his sudden death shortly after the meeting. His name will endure to signify a landmark in the history of the physiology of vision.



## NOTES

## Honours

SIR STEWART DUKE-ELDER delivered the Donders Lecture and received the (quinquennial) Donders' Medal at a meeting of the Dutch Ophthalmological Society at Utrecht on December 14.

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Prize of the  
International Association  
for Prevention of  
Blindness

AN honorarium of 1000 dollars to promote research work on ophthalmology is offered through the American Members of the Staff of the International Association for the Prevention of Blindness, the Jury to consist of the Executive Committee together with the President and the Officers of the Association.

The award will be made in connection with the XVIth Concilium Ophthalmologicum. Papers may be presented by any responsible research worker. The subject is to be *simple non-inflammatory glaucoma* and may include anything definitely relative to the question. The matter must be new and of such value; in the judgment of the jury, as to merit this recognition. Papers may be written in English or French; they should be those heretofore unpublished or those published between this date and October 15th, 1949. They should be in the hands of the secretary of the International Association for the Prevention of Blindness, 66, Boulevard St. Michel, Paris, through whom they will reach the Members of the Judicial Committee, not later than October 15th, 1949.

The decision of the Jury will be final.

\* \* \* \*

University of Glasgow  
Post-graduate  
Medical Education  
Committee

A systematic course in ophthalmology will be conducted from January 12 to June 11, 1948. The lectures will be given thrice weekly at 5.15 p.m. in the rooms of the Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow. Fee twelve guineas.

Those wishing to attend should make early application to the Director of Post-Graduate Medical Education, The University, Glasgow, W.2., from whom further particulars may be obtained.

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Compensation under  
the National  
Health Service Act  
in regard to  
Specialist practices

THE Ophthalmic Group Committee state that some confusion exists in the minds of Ophthalmic Surgeons in relation to compensation under the National Health Service Act.

Under the Act the sale and purchase of general practices is prohibited, but the position in so far as speciality practices are concerned remains unaffected. In future years it will be much more difficult to sell specialist practices and this has been plainly stated to the Minister of Health. He "adheres to the position, and as nothing is at present in the Act to disturb the selling, there can be nothing in the Act to compensate for the loss of the right to sell."

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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## *Assistant Editor :*

H. B. STALLARD

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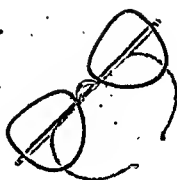
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LONDON:

THE BRITISH JOURNAL OF OPHTHALMOLOGY LTD.

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TO HIS MAJESTY  
KING GEORGE VI



TO HER MAJESTY  
QUEEN MARY

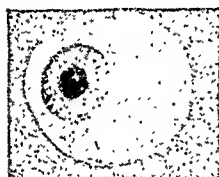
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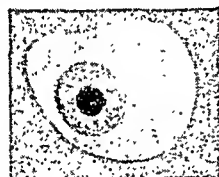
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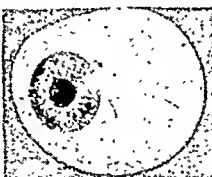
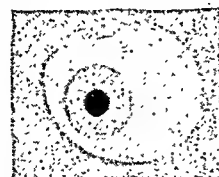
## ARTIFICIAL EYES IN PLASTIC



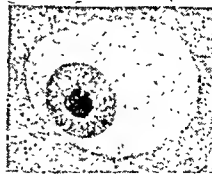
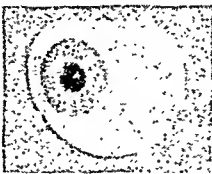
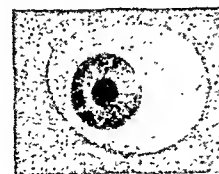
**A**RTIFICIAL eyes made by the new acrylic process have many advantages over those made of glass. They are more life-like in appearance, more comfortable in wear, are not affected by the secretions of the orbit, and above all they are unbreakable. They are also more easily alterable. Difficult shapes (necessitated by war injuries, burns, etc.), or thin shells to fit over shrunken globes, almost impossible to produce in glass, are quite possible in plastic.



Hamblins plastic eyes are made in plastic throughout, no paper or glass or indeed any non-acrylic substance being incorporated. Stocks of ready made eyes are available at Wigmore Street or at the provincial branches from which selections can be made. For more difficult orbits special eyes



can be made with little delay. For these a careful mould of the orbit is taken from which the eye is made and a special iris is produced to match the existing eye. In such cases a second visit is necessary for fitting.



15, WIGMORE STREET, LONDON, W.1

AND AT

MANCHESTER, LIVERPOOL, SHEFFIELD, LEEDS, EDINBURGH,  
NEWCASTLE-UPON-TYNE, BOURNEMOUTH, WINDSOR, KINGS LYNN

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

FEBRUARY, 1948

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## COMMUNICATIONS

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### THE SURGICAL TREATMENT OF PTERYGIUM\*

BY

ARTHUR D'OMBRAIN

SYDNEY, N.S.W.

OF recent years investigations into the pathology and aetiology of pterygium have shed much light upon the true nature of this condition. It is about eight years since it was brought to my notice that some American surgeons regarded the sub-mucosal portions of pterygium as the active part of the process; I learnt that after shaving the head of the pterygium from the cornea, they then dissected and excised the sub-mucosa from the under surface of the conjunctiva before transplanting the head. At the time, although I had been operating upon pterygia for some fifteen years, I was in a state of some concern about my results and had already made one modification in the McReynold's operation, in an attempt to reduce the proportion of recurrences. This first

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\* Received for publication, November 26, 1947. N.B.—The first draft of this paper was submitted to the Editors in the early summer of the year 1946. Unfortunately it was lost in transit to the printers.

modification was the deliberate leaving of a bare area of sclera between the corneal margin and the edge of the downturned conjunctiva, instead of approximating this edge to the cornea. The objective was to give the raw corneal surface time to heal before the conjunctiva grew up to the limbus again.

This modification improved my results but there were still recurrences. Adoption of the American idea of a complete dissection and excision of the whole of the sub-epithelial tissues underlying the affected area of conjunctiva, in conjunction with the leaving of a peri-limbal strip bare of conjunctiva, practically eliminated recurrences, as well as making the transplantation a comparatively flat procedure instead of a thick lump, for the transplanted or tucked tissue consisted now of the thickness of the epithelial or mucous layer only.

During the course of my experiments in the evolution of a more efficient operation, I had tried a certain number of simple excisions of the head of the pterygium, without transplantation. These simple excisions were about 70 per cent. successful as regards non-recurrence.

When, however, to the principles of excision of the head, and the leaving of a peri-limbal bare strip some 4 mm. in width, there was added the technique of complete dissection and excision of all underlying sub-mucosal tissue, right back to the caruncle, uniform success came my way at last and has remained with me for the past seven or eight years. Before describing in detail the steps of the operation I will make some reference to the nature and cause of pterygium.

To my mind the best discussion of the nature of pterygium ever written is the brilliant paper by Dr. Sabri Kamel in the *Brit. Jl. of Ophthal.*, of September, 1946, and I would hesitate to speak further on the subject except for the fact that my not inconsiderable experience in this field (some 1,500 operations) only serves to confirm Dr. Kamel's masterly synthesis and, in one or two items, to add to it.

Kamel maintains that pterygium is an irritative disease due to exposure and not primarily a degeneration. With this I quite agree, but would stress the fact that it is secondarily a degeneration. The older authors, notably Professor Fuchs, considered pinguecula to be the forerunner of pterygium and both to be degenerations. As I say, I consider Kamel to be more accurate in diagnosing an inflammatory origin but with the conception of the identical nature of pinguecula and pterygium I am in entire agreement, despite those who claim to have observed pterygium in the absence of pinguecula. The explanation of this, in my opinion, is simple, for I believe pinguecula and pterygium to

be, essentially, one and the same process aetiologically, anatomically and pathologically. What has been taken to be a pterygium in the absence of pinguecula is, in my opinion, simply a pinguecula situated at or in contiguity with the corneal limbus.

The pathological anatomy of pinguecula is that of a dense mass of fibrous tissue undergoing hyaline degeneration with deposition of amorphous hyaline material and excessive development of yellow elastic tissue. In its terminal stage it is a kind of localised tissue death, paralleling the displacement of normal connective tissues by excessive accumulation of elastic tissue found in old age in any part of the body's connective tissue strata. But, in pinguecula, old age is not a predominating factor; on the contrary, in Australia at any rate, pinguecula occurs in great frequency in young adults and even in adolescents. There must, therefore, be some other explanation or, perhaps it would be more accurate to say, some additional explanation than that of senility.

The stroma or sub-conjunctival portion of pterygium presents a similar histo-pathological picture to that of pinguecula, namely, an extensive aggregation of fibrous tissue containing numerous elastic fibres and patches of amyloid and hyaline degeneration. But as Kamel points out, when this contracting fibrous tissue becomes anchored at one end to the unyielding corneal tissue, the looser conjunctival tissue becomes pulled towards the cornea.

The cornea itself becomes involved in the inflammatory process and also in a secondary degeneration, with the presence of elastin, down to and including Bowman's membrane.

In optic section from the slit-lamp, the sub-mucosal portion of both pterygium and pinguecula shows up as a raised gelatinous-looking mass of greyish-yellow colour, interspersed with yellow, grey and white granules. Even in the corneal portions of pterygium, behind the grey apical extremity, optic section shows a yellowish tinge due to elastin in the deeper epithelial layers.

As is well known, the first corneal changes (best observed with the slit-lamp microscope) consist of grey patches at or slightly anterior to Bowman's membrane. The number and forward extension of these isolated patches form a useful guide to the activity of the process; when many and far advanced and especially when vascularised, the pterygium is active; when few or absent beyond the grey apical border of the growth, the pterygium is not in a state of rapid expansion.

It has long been recognised that climate is the main predisposing cause of pterygium, but it has not been so widely emphasised that the same applies to pinguecula. Most European authors stress senility as the pinguecula's main cause; as has been stated above, in Australia pinguecula is extremely common in young adults and not rare in adolescence.

The high incidence of pterygium in hot countries led most of us to assume that its occurrence was in direct ratio to the heat of the climate. However, a few years ago investigations carried out by some American ophthalmologists showed pterygium to be no more frequent in the hottest States than in others. Later, observers in both America and Australia (notably Banks Smith and Frank Flynn) have found an association between pterygium and the water vapour content of the atmosphere; where the humidity percentage is high, pterygium is less common than in places where the average annual percentage is low.

It would thus appear that pterygium is a reaction to the irritation of dry, hot, dusty atmospheres; its location in between the upper and lower lids, and particularly in the medial area where there is *an anatomical pocket formed by the nasal, frontal and malar bones*, gives credence to this view. Moreover, the bulbar conjunctiva lateral to the cornea, situated as it is immediately below the lacrymal gland, receives the tears first and freshest.

I have pinguecula in both eyes; they formed in my twenty-second year when I possessed my first motor bicycle and before I learnt the wisdom of wearing goggles; my late father, an ophthalmic surgeon, noticed the pinguecula and made me wear goggles. The pinguecula are situated midway between the limbus and the plica semi-lunaris and so far I have no pterygium but I have seen many hundreds of cases of pinguecula spread to the limbus and become pterygia.

Here then are two conditions of the same histological and bio-microscopical appearance, derived from a common cause and differing in site only as to whether they are or are not in juxtaposition to the corneal limbus. Those that are not or do not become contacts with the limbus remain pinguecula. Those that do, progress to the formation of pterygium. If this assumption is correct, it is of some academic interest but it is of far greater surgical interest. For if the essential portion of a pterygium is sub-epithelial, then surgical treatment must aim at the removal of the active connective tissue core and not be content with mere transplantations, however ingeniously devised. A recurrent pterygium is a major ophthalmic problem, often necessitating the use of skin or mucous membrane grafts. It is, therefore, important to succeed at the first attempt on every pterygium operated upon.

Dr. Kamel, in his procedure of applying carbolic acid to the under surface of the pterygium, is attacking the core of contracting fibrous tissue, but it would seem to me more logical and more surgically complete to dissect it all away. At all events, using my present method of combined corneal shaving, stripping of

the subconjunctival core and exposure of a bare peri-limbal zone. I have had no post-operative recurrence for the past seven years.

The steps in the operation, together with the reason for each, are now described.

1. A horizontal incision is made with scissors in the bulbar conjunctiva above the upper border and below the lower border of the pterygium, from the limbus nasally for five millimetres. This incision is to ensure the creation of a peri-limbal strip bare of conjunctiva. The leaving of a strip of bare sclera, though it may seem an unsurgical procedure, is one followed independently by other workers (Colvin, Candlish, Accola), and is designed to give the cornea time to heal before conjunctiva grows across to the limbus. If conjunctiva is drawn right up to the limbus at the conclusion of a pterygium operation, there is a danger that the free edge may adhere to the raw corneal surface left by the removal of the apex of the pterygium, with consequent early recurrence.

2. The closed scissors are pushed downwards through the upper incision and beneath the pterygium tissue, in preparation for the next step.

3. One limb of a small dressing forceps is inserted either through the upper or the lower incision, so that the pterygium tissue may be firmly held between the forceps limbs inside and outside the tissue. This firm grip near the limbus prevents tearing of the conjunctiva.

4. With a sharp cataract knife or keratome, the apex of the pterygium is shaved from the cornea, a thin layer of cornea being included in the shaving, for the corneal part of a pterygium is essentially a degeneration of the cornea; also it ensures complete removal of all the conjunctival tissue with its blood vessels.

5. The apex of the pterygium, now free, is grasped at its tip by fixation forceps and held up vertical and taut by an assistant. The surgeon, using fine dressing forceps or iris forceps and sharp pointed scissors, dissects the whole sub-conjunctival portion of the pterygium from the under surface of the epithelial layer, as far medially as the plica semilunaris. This comes away in one triangular piece and is a remarkably thick and extensive structure, underlying the whole extent of the pterygium. Indeed, in my view, it is the pterygium, and its removal is essential. In addition, its absence makes the remaining conjunctival layer a thin one and avoids the lumpy and unsightly appearance left by the orthodox transplantation operation. I agree with Dr. Kamel that transplantation is illogical and quite unnecessary.

6. At the completion of these procedures, the free edge of the conjunctiva is trimmed so as to excise a sliver of it, and thus



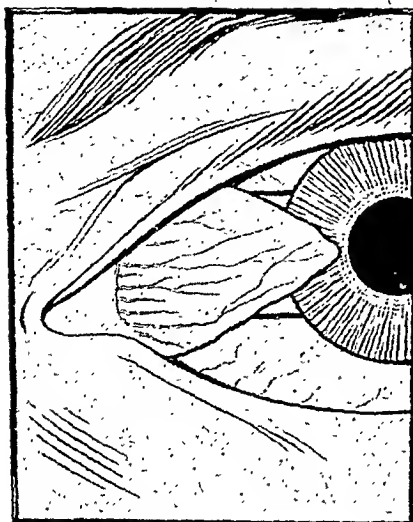


FIG. 1.

Showing initial horizontal incisions in the conjunctiva, above and below the pterygium.

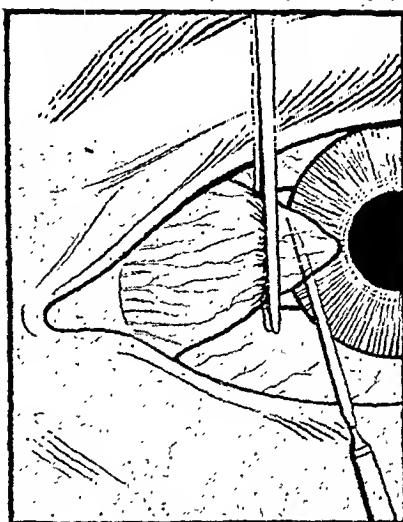


FIG. 2.

Showing the neck of the pterygium firmly held between the forceps blades, while the apex is being shaved from the cornea.

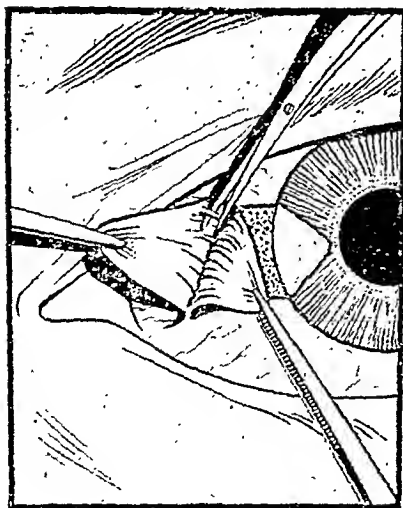


FIG. 3.

Showing the sub-conjunctival tissue being dissected away, prior to its excision.

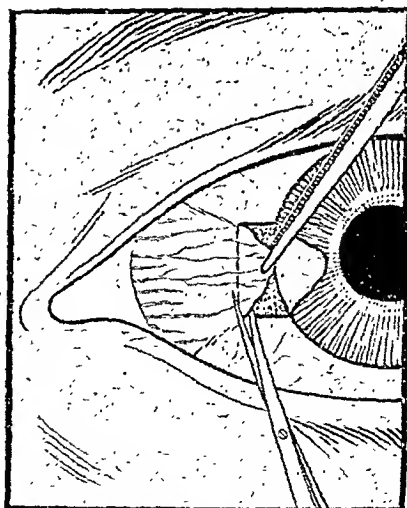


FIG. 4.

Showing the apex being trimmed off by scissors in the direction indicated by the dotted line

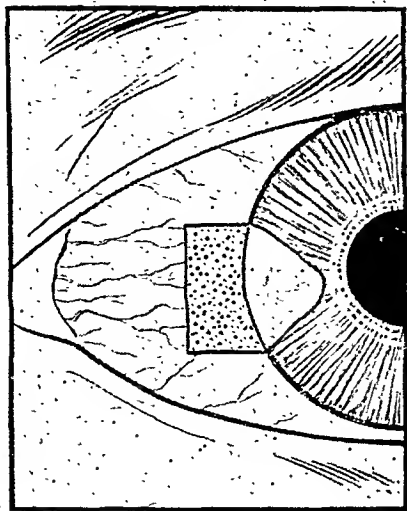


FIG. 5.

Showing the quadrilateral of bare sclera, left at the termination of the operation.

leave a bare strip of sclera several millimetres in width. The conjunctiva rapidly grows over the scleral strip but not before the corneal surface has healed.

7. Before bandaging the eye, as well as antiseptic drops, atropine 1 per cent. should be inserted to help the cornea to heal.

This technique may be successfully used in recurrent pterygium but in cases of second recurrence the free graft method as described by A. L. North should be used. In this procedure a strip of skin is slid under the conjunctiva above and below, separating the free conjunctival edge from the cornea until the latter has healed, an application of the same principle as the bare scleral strip in the operation I have described. The reason for using the graft in second recurrence cases, instead of using the technique described in this paper, is this; in such cases the sub-conjunctival adhesions are of such density and toughness that tissue planes are lost and there is danger of actually perforating the sclera if dissection or even separation of the pterygium tissues from the sclera is attempted. This disaster once happened to me and taught me a salutary lesson.

In conclusion, argument has been presented for the view that pinguecula and pterygium are fundamentally identical aetiological and structurally, that the primary focus of activity is in the connective tissue and that efficient pterygium surgery must include removal of this tissue, the technique for which has been described.

*Acknowledgment.*—Abbott Studios, Sydney, for their careful illustrations.

## THE ORIGIN OF THE MALIGNANT MELANOMATA\*

BY

EUGENE WOLFF

LONDON

It is presumption on my part to cross the Border into the land of Dawson and his great work on the melanomata and read a paper on that very subject.

I would, however, like to say at the outset that I owe all my basic knowledge of our problem to him; and it must be remembered that Dawson himself hoped his work would be made the stepping-stone for further investigation. It seemed to me also that it was perhaps opportune to try and sum up the valuable, and I would say indispensable, evidence which ophthalmic pathology furnishes.

Ribbert a long while ago showed that malignant melanomata could arise from branched chromatophores, and it has now been confirmed many times that a teased preparation of what on microscopic section appears to be a spindle-celled tumour of the choroid is in fact composed of chromatophores in all stages of development. The most important fact brought about by Ribbert's work was that in secondary nodules found in the brain and liver the cells were identical with choroidal chromatophores. Having proved this point the unfortunate thing is that he then attempted to show that all melanomata had this origin.

Similarly Unna and Dawson found that these tumours could arise from downgrowths of the surface epithelium. This, too, has been confirmed time and time again. But they then attempted to prove that all malignant melanomata arose in this way.

Lastly Masson has brought forward evidence to show that the much disputed naevus cells are really developed from the end apparatus of the sensory nerves. As a result of this it is now very widely held that all pigmented growths have a neurogenic origin. It is one of the main purposes of this paper to attempt to show, what indeed has been done before, that a unitary theory both of the origin of melanin and of malignant pigmented growths is not tenable.

It is essential for our purpose to decide on a proper definition of what is meant by a naevus cell; for some say they are large and others small; some describe them as clear, others dark. I agree with the following which is that of Dawson:—Naevus cells

\* Being the William Mackenzie Memorial Lecture read at Glasgow on October 24, 1947. Received for publication, December 8, 1947.

(Figs. 1, 2, 3, 4, 5) are small, almost atrophic cells, polymorphic in outline with little cytoplasm. They are separated by a varying amount of connective tissue from each other and are usually arranged in what are termed cell columns or groups or nests which are separated from each other by fibrous tissue septa and the whole usually from the epidermis by a narrow zone of almost homogeneous connective tissue. It was the arrangement of the



FIG. 1.

Conjunctival naevus at limbus. Note dark staining nuclei of naevus cells and downgrowths of epithelium. An island of epithelial cells among naevus cells.

cells in columns and groups that first led von Recklinghausen to trace their origin to the lymph-channel endothelium. The naevus cells as they grow older tend to resemble lymphocytes and may become drawn out into filaments.

The main reason for deciding at the outset what we mean by a naevus cell is that we may distinguish them from epithelial cells derived from the downgrowths of surface epithelium. I believe this to be of vital importance and yet, very curiously, it is only very rarely discussed even in the most important works on the subject.

As a rule it is quite easy to distinguish naevus from epithelial

cells. So long as the epithelial cells are part of the club-shaped downgrowths there is, of course, no difficulty in differentiating them from the naevus cells. This also applies to islands of epithelial cells found as a result of the epithelial columns being cut across. Also the central portions of the epithelial downgrowths may degenerate and then a cystic condition is produced (naevus glandulosus cysticus). Although often described I have

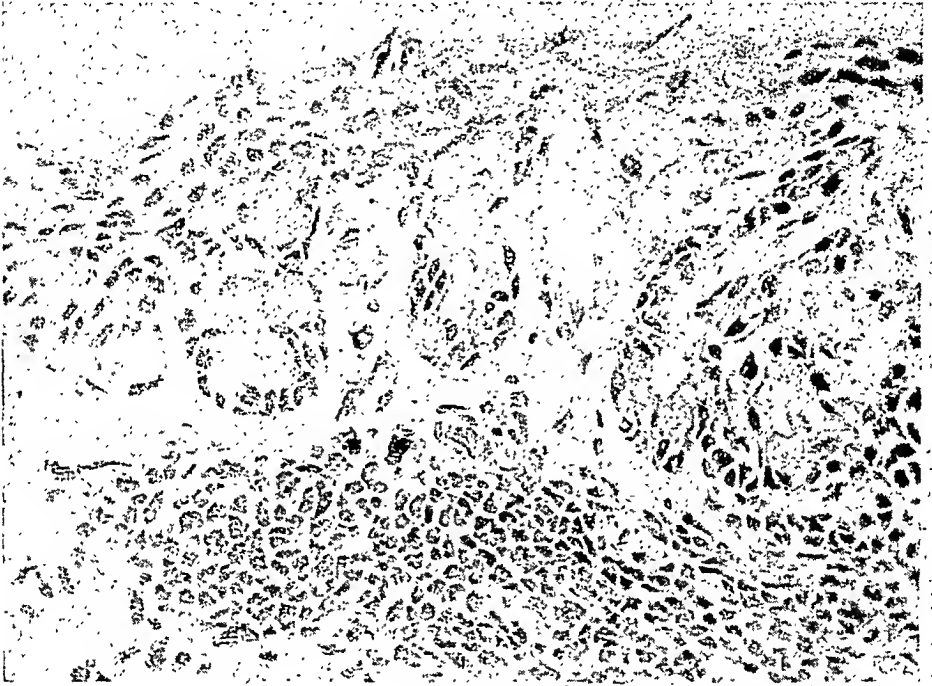


FIG. 2.

FIG. 1 under higher power. Arrow points to process of a chromatophore.

never seen such a cystic tumour formed as a result of degeneration of the naevus cells. When the epithelial cells no longer form part of the downgrowths or of the islands they are differentiated by the characteristics of the cells themselves. The typical epithelial cell has a large vesicular nucleus staining much paler than that of the naevus cell. Also it has an abundant cytoplasm. In certain cases the proliferating epithelial cells are fairly closely packed and then one has to rely on the staining properties of the nucleus only to differentiate them. But where there are masses of the two types of cells next each other the difference between the paler epithelial nuclei and the darker nuclei of the naevus

cells is very striking (Fig. 4). It will be noted as in Fig. 4 that epithelial and naevus cells may proliferate side by side in the same tumour. This fact, provided one is not wedded to a unitary theory for the origin of these growths, is obviously of great importance. A very important point which applies only to conjunctival naevi is that the downgrowths of epithelium may contain mucous cells (Fig. 7). Indeed, P. Veil in his *thèse de*

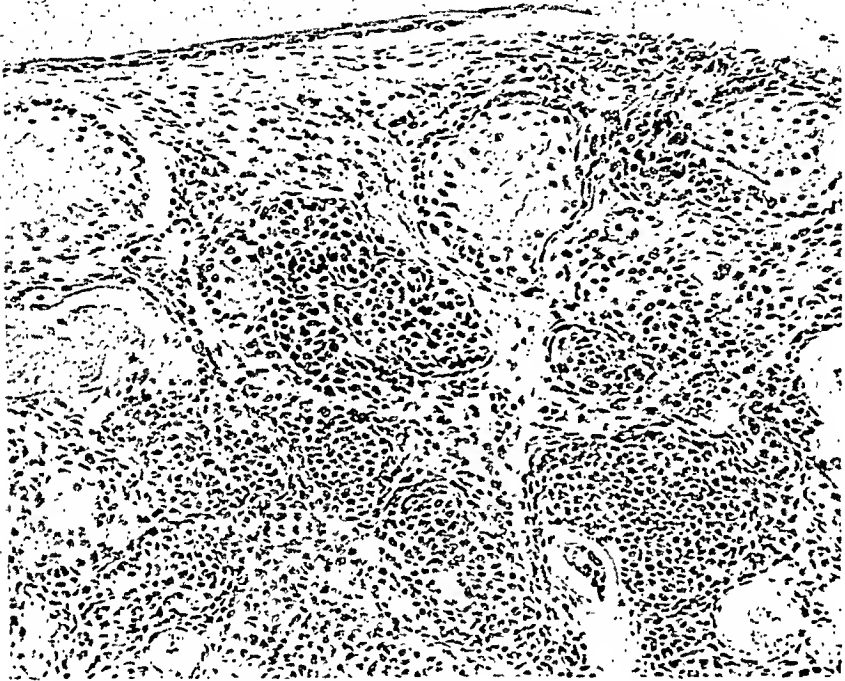


FIG. 3.

Conjunctival naevus. Note islands of epithelial cells and nests of naevus cells.

Paris goes so far as to say that because there are mucous cells among the naevus cells therefore these latter are epithelial in origin! But at any rate the mucus stamps the cells as epithelial.

As stated above, it is usually easy to distinguish naevus from epithelial cells; but at times, owing possibly to the method of fixation and staining, it may be very difficult or impossible.

The epithelial theory of origin of the naevus cells is usually said to have received important support from the work of Bruno Bloch, who treated sections of normal skin with dopa and found that the basal layers of the epithelium were coloured grey or

black; the branched intra-epidermal cells of Langerhans being particularly dark. Also in the masses of naevus cells the superficial ones gave the dopa reaction. This colouration was held by Bloch to be due to the formation of dopa-melanin resulting from the presence of dopa-oxydase in the cells. All cells giving this reaction were held to be capable of producing melanin and were therefore melanoblasts. But while in general Bloch finds

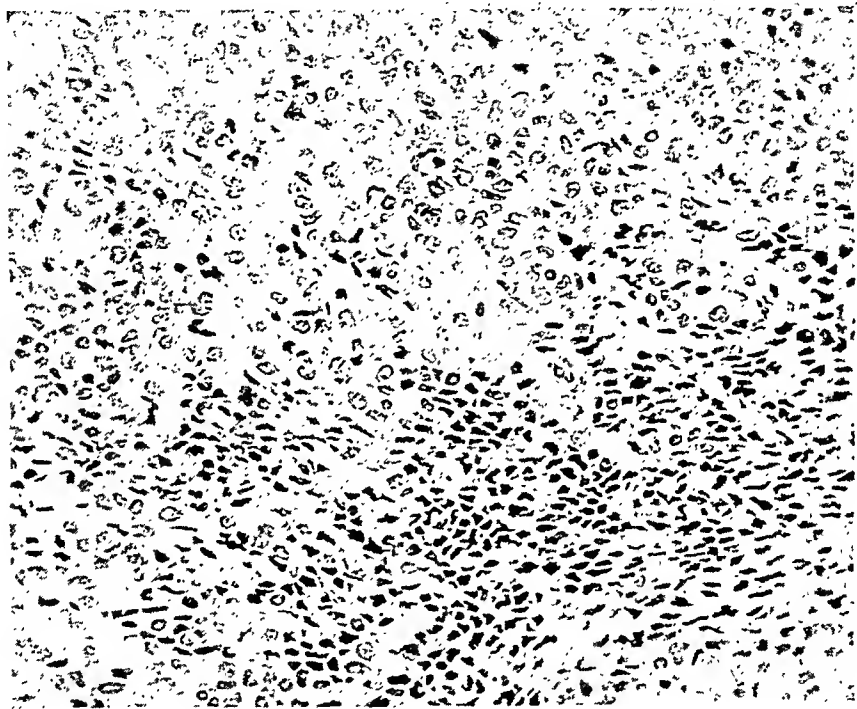


FIG. 4.

Deeper portion of same tumour as FIG. 3. *Note*: proliferation of naevus cells (dark nuclei) and epithelial cells (pale nuclei) side by side in same tumour.

no cells of the normal dermis to be dopa-positive the cells of the Mongol spot are. Now the Mongol spot in the sacral region consists of branched chromatophores like those of the choroid and generally recognised as mesodermal in origin. In making this exception, therefore, Bloch in fact helps to prove the dual origin of the pigment.

It is often stated that the problem of the origin of the malignant melanomata is synonymous with the problem of the origin of the naevus cell. This I believe is a fundamental error and has led to a great many unjustified conclusions. In the first place it

cannot be too strongly emphasised—a point that is often forgotten—that although there are naevi in the uveal tract there are no naevus cells. In fact, Morax would regard the naevi of the skin and conjunctiva as quite different tumours from those of the uvea. Also we find that Bloch, like so many others, having decided that the naevus cells are epithelial in origin makes no distinction between them and the epithelial downgrowths. You

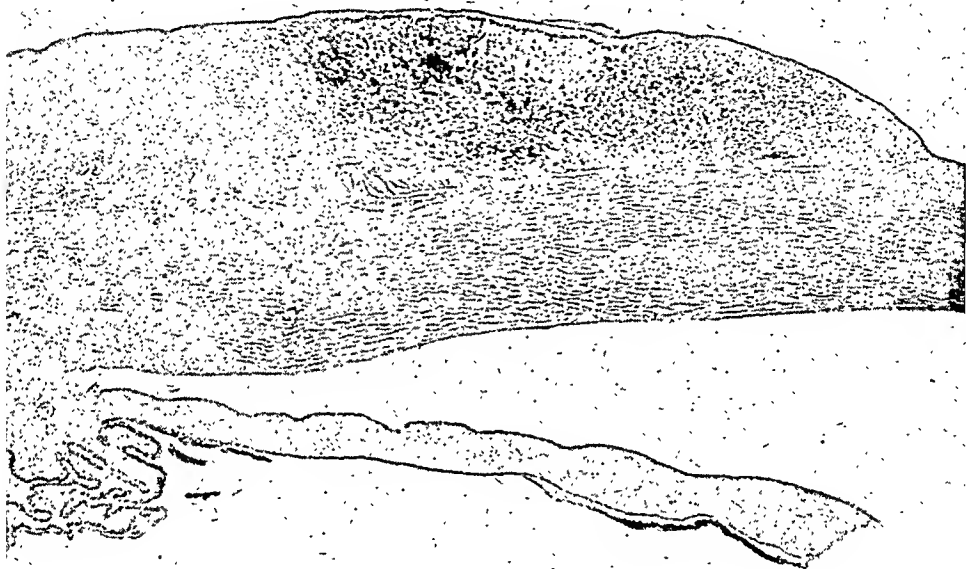


FIG. 5.

Melano-carcinoma of limbus. Note growth adherent to anterior surface of cornea.  $\times 25$ .

will see by the figure taken from Bloch's article in the Jodassohn Handbuch that he describes an obvious downgrowth of epithelium as consisting of naevus cells.

Further, Dawson's well-known figure of the formation of a malignant epithelial pigmented growth shows this arising from downgrowths of epithelium and not from naevus cells.

I would next like to draw attention to a paper by D. T. Smith in the Bulletin of the Johns Hopkins Hospital for 1925, which I think has received nothing like the attention it deserves. After pointing out that if pigment is formed in a cell the granules are the same size, he says: "When granules of pigment were taken in by cells not normally pigmented, the picture was distinctly



different from that described above. In this case the pigment was a foreign body in the cytoplasm, and the cell reacted in such a manner as to clump it into masses of irregular size and shape. Cultures of various types of embryonic chick cells were grown and pigment granules then added to the culture fluid. The whole process of ingestion and clumping of the granules into masses in the cytoplasm, with the formation of a vacuole about each



FIG. 6.

Detail of Fig. 5 under higher power. Note formation of theca containing *epithelial* cells and the place where the epithelial cells have grown down through basement membrane (Zenker Mallory's triple stain).

mass, could be followed with the microscope (Smith, 1921). The reaction was always the same, regardless of the source of the pigment. Melanin granules from the eye (chick, pig, dog or human), carbon particles, carmine granules, indian ink and blood pigment, all became clumped in the cytoplasm into masses of irregular size and shape. When once the pigment had been taken into the cytoplasm it was not given up until death of the cell.

"It is evident from these observations that here is a practical method of determining from the appearance of the granules, when examined with the oil immersion lens, whether they have been produced by the cell or have been taken in as foreign bodies. In studying the pigment cells we need no longer be confused by the question whether a particular cell under observation is a pigment producing or a pigment carrying cell."

Dawson and others, in order to bring the origin of the choroidal melanomata into line with the epithelial theory, have suggested

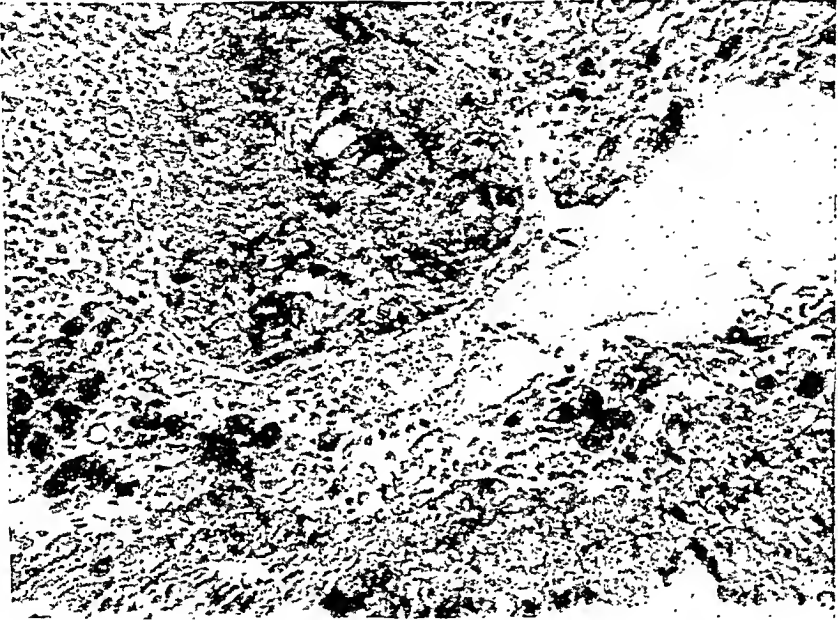


FIG. 7.\*

Section of naevus of conjunctiva to show mucous cells (stained green), both in surface epithelium and in epithelial downgrowth (Masson's stain).

that the choroidal pigment was derived from the retinal pigment epithelium. As has now often been pointed out there is a great deal of evidence which makes this impossible, or at any rate extremely unlikely.

In the first place the retinal pigment is morphologically different from the choroidal. The retinal pigment most characteristically occurs as spindles or rods; it is true that in the bases of the cells rounded forms are found, but these are much larger than the fine particles in the choroidal chromatophores. Also the retina is fully pigmented by the fifth month of intra-uterine life, whereas no pigment occurs in the choroid till a few months before birth, and then first in the outer layers. Treacher Collins showed, too, that the pigment epithelium of the retina though amoeboid

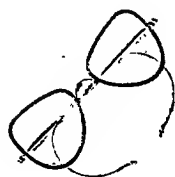
\* Unfortunately reproduction in monochrome does not show the difference.

throughout life does not pass through the membrane of Bruch. He also brought forward evidence to show that the uvea produces its own pigment: tags of pupillary membrane which have been completely isolated before the ingrowth of the secondary optic vesicle may become normally pigmented; and in rudimentary eyes in which no epiblastic tissue was present the uvea was found normally pigmented. Then, too, it has been repeatedly shown that in tissue culture the retinal pigment cells grow out in sheets like epithelium while the choroidal chromatophores grow like fibroblasts, *i.e.*, as isolated cells. Lastly, the choroidal pigment particles are all the same size. According to Smith, therefore, the pigment has formed in these cells which are therefore melanoblasts.

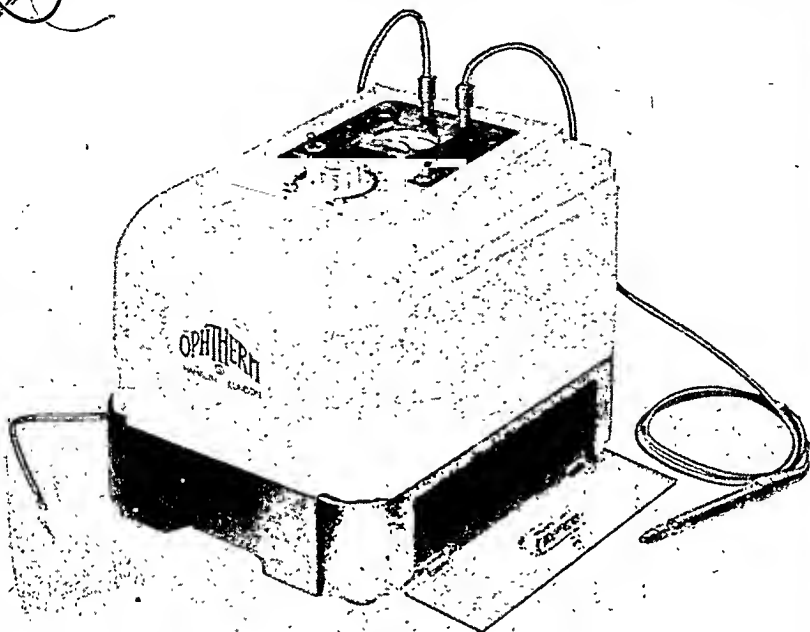
As further evidence against a unitary theory of the origin of malignant melanomata I would remind you of the well-known difference in the method of growth between the sarcoma and carcinoma or epithelioma of the limbus. The epithelial tumours tend to grow over the cornea like a pannus being closely adherent to it; while the sarcoma usually forms a mushroom-shaped pedunculated growth which tends to cover but not to get adherent to the surface of the cornea.

We now come to a consideration of Masson's neurogenic theory. This is a beautiful, detailed and suggestive work which has received almost universal acceptance. The following points also seem to favour it: The association of neurofibromatosis with café-au-lait spots and pigmented growths; the interesting demonstration by Laidlaw and Murray that naevi probably represent the touch corpuscles of reptiles and amphibia; the suggestion latterly put forward that the pigment cells are derived from the neural crest and grow down with the nerves to the skin, etc., and finally, possibly the curious insensitivity of pigmented growths to X-rays. But there are a number of important facts which call for criticism. In the first place, and this is a fundamental point, the theory has no room or explanation for the downgrowths of epithelial cells, both in the naevus and in the malignant melanoma. Thus in agreeing with Masson's theory Boyd in his excellent Pathology says: "In many cases there is an apparent proliferation of the basal layer of epidermal cells with the formation of downgrowths of cells which penetrate into the dermal portion of the naevus and thus gives the impression that the tumour has arisen from the epidermis. It seems more probable that these basal epithelial cells are merely pushed aside and displaced downwards by the proliferating naevus cells and melanoblasts originating in the epidermal portion of the sensory organs."

Now there is in my preparations no evidence that the epithelial cells are pushed down. They grow and proliferate as typical epithelial cells.



## OPHTHALMIC DIATHERMY (THE OPHTHERM)



The apparatus illustrated above has been designed and specially developed for retinal detachment operations.

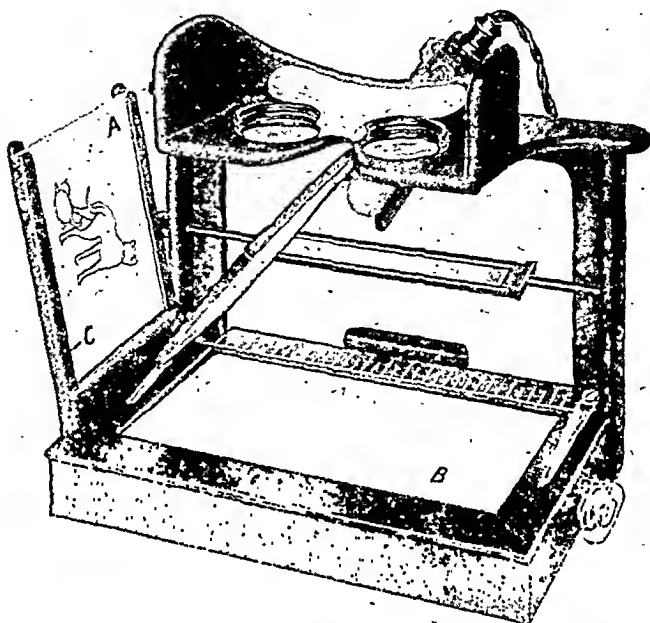
It is of the spark-gap type ; the gaps being laboratory set and needing no subsequent readjustment.

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In the second place Masson says that the cells of the Merkel-Ranvier corpuscles are represented in the human by the clear cells (*cellules claires*) and what he calls the branched pigmented Langerhans cells and that these are therefore really modified cells of Schwann. Now the clear cells occur at regular intervals at the junction of the dermis and epidermis. They have a rounded or kidney-shaped nucleus which stains denser and is larger than that of the neighbouring epithelial cells. Around this is a well-defined clear space. From the base of the cell Masson describes a process which, continuous with a nerve fibre, runs down into the dermis. Masson holds that the clear cells are derived from Schwann cells, which migrate and insinuate themselves between the epithelial cells of the basal layer during foetal life.

Now up to the present there has been no embryological proof of this. Also it has been shown that after the destruction of certain sense organs, for instance the Gandry corpuscles of the duck, the cells of these are regenerated locally and not from the nerve fibres; and further the cells of the Merkel-Ranvier bodies appear to be developed from the surface epithelium and not from the cells of Schwann. (Szymonovicz).

Also Masson describes the Langerhans cell as a branched pigmented cell lying in the basal layers of the epidermis and sending processes into the dermis. It must be clearly understood, however, that the cell Langerhans described has only been demonstrated with gold chloride and lies 3-5 cells up from the basement membrane. It has never been shown to have a nucleus and Langerhans insisted that it had nothing to do with pigment function.

Masson believes that what he calls the Langerhans cell\* is the sole producer of pigment and that it acts like a gland pouring its pigment into the neighbouring cells. But Smith has shown that the pigment granules in the basal cells are small and rod-shaped, while in the Langerhans cells the pigment is rounded; moreover they are all of the same size and therefore formed primarily in the epithelial cell.

A great difficulty also arises from the fact that Masson does not say whether these tumours are mesodermal or ectodermal. This naturally follows from the fact that there is still dispute as to the origin of the cells of Schwann. Many of those who uphold the neurogenic theory, however, use such terms as neuro-epithelial and neuro-sarcoma.

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\* I find however, that this is now the accepted meaning of the Langerhans cell and must presumably remain so.

Further, the neurogenic theory is another attempt at bringing all pigmented tumours under one roof, and as such it cannot be accepted.

Next I would refer to those rare but definitely established growths which arise from the pigment epithelium of the retina, ciliary body and iris.

Only one, that of Griffith, has been described as arising from the pigment epithelium of the retina; a fair number have been found coming from ciliary epithelium, the best known being that of Treacher Collins, which was later included in the work of Fuchs.

A number of growths also have been described arising from pigmented epithelium of the iris. I show you the picture of Morax's case. The actual growth is dense black; a bleached section shows that the growth is composed of cells exactly like those of the pigment epithelium of the iris. Here then we have pigmented growths arising from epithelium. There can be no question of their coming from sensory nerve endings.

We see then that melanomata may arise from naevus cells, epithelial cells and from branched chromatophores and, as in Fig. 4, naevus and epithelial cells may proliferate side by side in the same tumour.

I would suggest, therefore, that the naevus should be regarded as a composite or mixed tumour consisting, for our purpose, of naevus cells, epithelial cells, and branched chromatophores. Each of these may proliferate alone or with the others and produce a malignant pigmented tumour. The final structure will depend on the relative proportions of the three types of cell.

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## "AN OCULIST IN SWITZERLAND"

BY

JOHN FOSTER

LEEDS

THE account which follows is a précis of lectures given on this subject at the Royal Society of Medicine and the Tennent Institute. It describes the Swiss portion of an ophthalmic tour in August and September, 1946. The kindness of the heads of the various clinics during the visit, and in responding to numerous enquiries subsequently, is a matter for which I would like to express my gratitude.

The writer doubts if it is possible to see so much of ophthalmic interest in so small an area in any other part of the world. Switzerland is not only a creative amalgam of three European civilisations, but is also endowed with a most excellent transport system, has had 122 years of continuous peace, and has a first-class precision engineering and pharmaceutical industry in addition.

## Basel

Professor Brückner, the head of the University clinic, is the Doyen of Swiss Ophthalmology, and retires on reaching the age limit in 1947. Born the son of a Russian Professor of Geography in Zoppot, he received part of his training in Berlin, partly as assistant to Hering at Leipzig, and later held the Chair at Jena. He came from this last city to the Chair at Basel, with an interest in physiological optics, and a wonderful collection of apparatus. He delighted his new assistants on arrival, by doing the first Krönlein operation ever seen in Basel (with a chisel), and still takes a poor view of what he calls "anterior chamber surgeons." Apart from a standard textbook, his chief publications have been on physiological optics (especially on dioptrics and colour vision), though there are many on clinical subjects.

His clinic of 74 beds is sixty years old; an excellent building by our standards, but considered out of date in Switzerland. His friend, the late Professor Bielschowsky, he says, described it as "like a sanatorium"—I suppose because there are many small high-ceilinged rooms.

The plans of the new clinic (of approximately the same beddage), will be available after the Basel Parliament has seen them in 1947.

On going through the clinic the orderliness is most striking—a room for foreign reprints, a library, a room for the Professor's



reprints, four chemical laboratories, and two for physiological optics.

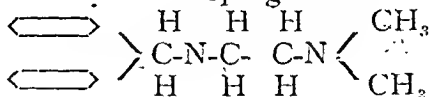
I spent an hour with Fräulein Giger, who runs the orthoptic department. She is a social worker who does this voluntarily in her spare time, including the necessary reading. She has a good grasp of the problem of "false projection," which is minimised by some continental schools in spite of Bielschowsky's teaching.

The professor, she says, is encouraging, but some of the younger men are not so interested. Although she has a Hamblin amblyoscope, more English apparatus would help. Most of her time is spent in treating amblyopia. The children put rings round dots of light on a board, and are admitted as in-patients for occlusion.

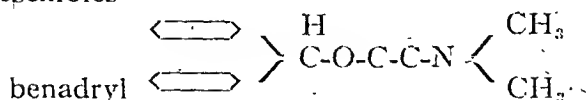
I also spent a similar period with the head biochemist. A good deal of research has been carried out here on the intra-ocular distribution of cholinesterase, so that they are particularly interested in the fluorophosphonates (which produce miosis by destroying it), though they have not actually experimented with them. As they agree with Ridley (*Trans. Ophthalm. Soc. U.K.*, Vol LVIII, ii, p. 590, 1938) that the source of the increased ocular histamine in glaucoma is the tears, they have been testing the conjunctival and corneal tolerance to "antispin."

$\text{H}_2\text{N} \cdot \langle \rangle - \text{S} \begin{array}{c} \text{N} \end{array}$  an anti-histaminoid. This substance

causes corneal oedema, but they are hoping for better results with neo-antergan.



which closely resembles



introduced here from America

for treatment of allergic conditions by mouth. They are also tracing the distribution of phosphorylated carbohydrates in different parts of the eye.

On a ward round the professor is followed by a sister with a tray of drop bottles and clean pads. He changes the pad and puts in a drop himself after examination. Squints tenotomised with a guard suture and intra- and extracapsular extractions side by side, were the only cases of note. As usual the intracapsulars were much "whiter" than the others.

I tried to obtain some idea of the organisation, standards, and methods of payment, in the University Clinics, in the incorrect

belief that there was a State Service. As Switzerland is cantonized, and each has a different system, the Professor told me it was impossible to generalise.

### Schaffhausen

I journeyed to Schaffhausen from Zurich by train (third class), and found the wooden seats quite tolerable for an hour or so. It is pleasing to find that while notices request abstention from spitting in French, German and Italian, it has not been found necessary to include one in English. Swiss-railways are superbly run, and the conductors most helpful.

Grieshaber cataract knives are so well known, that I was surprised to find their factory to be a small cutler's shop.

The firm produced their first eye instruments in 1915, when the French supply failed. Even their initial efforts were a good deal superior to the French, and a challenge to the English, while certain instruments cf. corneal trephines are superior to our own products. So good is the fit of the obturator of a Franceschetti trephine that when it is pushed home the instrument looks like a solid rod to the naked eye.

Grieshaber's supply stainless steel knives ("Rostfrei" or "Innoxidable") in preference to those of silver steel to most Swiss clinics, as they claim there is little difference in the quality of edge, and this material if sterilised by hot air eliminates the problem of rust.

Against this, I found three out of five Universities sterilise their knives chemically, and I suspect some other factor, for example the smoke (acid) free Swiss air may also play a part.

London surgeons sometimes claim that the close limits to which Grieshaber instruments are specified indicate automatic rather than manual reproduction. The firm is unwilling to say whether this is so or not, as it is a trade secret.

On the other hand, the introduction to their 1946 catalogue states that instruments are "exécutés à la main," and the appearance of the ground zone of the Grieshaber knives made in U.S.A. by a cousin of the family differs from that of the Swiss product.

Their most interesting instruments are those for keratoplasty, and I would advise those wishing to examine them to write in advance as:—

(a) certain scissors forged in Germany, and finished in Schaffhausen, are no longer available.

(b) the firm do not always "carry" their full range cf. Giradet's instruments, and only make some of them to order.

(c) some of the instruments have several uses, and discussion about them in a foreign language can be most confusing. For

example, Franceschetti's "niblick" (Fig. 18*b*) can be used for both keratoplasty and dacryocystorhinostomy; and Elschinig's round-ended knife (Fig. 18*a*) for removing the remains of Descemet's membrane was originally designed to extend cataract sections, and is still so employed.

### Zurich

An excellent account of Professor Amsler's clinic has been given in the *Brit. Jl. of Ophthal.*, Vol. XXXI, p. 223, 1947. This is the largest clinic in Switzerland, and as will be observed from Roper Hall's account, some most interesting research work has been and is still being carried out there.

### Berne

The clinic is a big one (70 beds), though Professor Goldmann's private work goes to a large nursing home, the other side of the river.

Professor Goldmann, who comes from Komotau in the Czech Sudetenland, was trained as a physiologist, and as in the case of Professor Brückner this perceptibly influences the trend of his papers.

Take, for example, "The Aqueous Veins," which he discovered shortly after, and quite independently of Ascher. He considers that pathologists failed to find these, as they are just like ordinary veins post-mortem.

Estimation of the total refraction (Gesamtbrechtkraft) of the eye and its comparison radiologically with its axial length, or the Stiles-Crawford effect—the apparent variation in intensity to an observer of a narrow beam of light according to the point at which it traverses the pupil. His experiments indicate that the latter is due to special properties of the retina rather than absorption by the transparent media.

For me the main interest of his work lay in his ingenuity in diagnostic instrument design, and the conclusions this has enabled him to draw on clinical subjects. He was kind enough to demonstrate the use of some of these devices, all of which are obtainable from Haag-Streit, Werkstätten für Präzisionsmechanik, Liebefeld-Berne.

*Localisation of intra-ocular foreign bodies and retinal tears.*—The mechanical basis of these three methods is a small metal ring whose under surface bears four obliquely directed hooks (Fig. 1). When this type of ring is applied by a twist of an applicator to a scleral or corneal surface, it adheres firmly without causing permanent damage, and can be removed when required by a twist the other way.

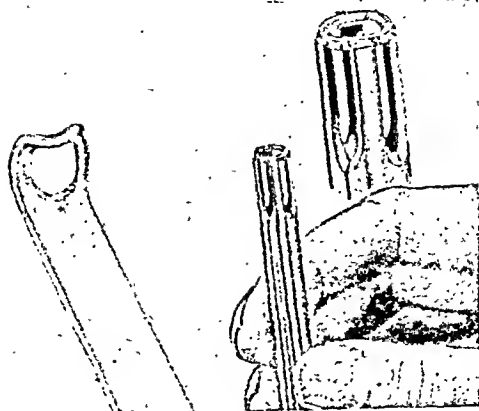


FIG. 1.

Goldmann's localising ring with applicator and plastic lid retractor.

*Initial localisation.*—The ring for initial localisation of intra-ocular foreign bodies, is about 9 mm. in diameter. Prior to application to the cornea its hooks are dipped in Indian ink.

The marks so produced serve as "points de repère" when the ring has been removed after the X-ray.

During radiography the lids must be held back by transparent and radiotranslucent plastic retractors, or they sweep the ring off.

*Non-magnetic foreign bodies.*—The majority of such bodies are embedded in, or close to the scleral wall, and a modification of the above technique has proved so satisfactory that 24 out of the last 25 such bodies have been successfully withdrawn by insertion of forceps through a scleral incision at the site so indicated.

The conjunctiva is reflected over the site indicated by initial localisation, and a 3 mm. hooked ring of the same type "screwed" on to the sclera at this point.

X-ray snapshots are taken with the patient on the operating table, the central X-ray beam being perpendicular to the plane of the ring.

The pictures are recorded on dental film cut down to an oblong of 1.5 x 4 mm., the open edge being sealed with strapping, and the tiny cassette so produced inserted in the finger of a rubber glove. The latter being sterilised can be held close against the sclera in the plane of the ring.

The ring is moved as the films indicate, until it overlies the foreign body.

Very rapid development is necessary in view of the multiple exposures, and is achieved by use of the following solutions:—

- A 500 c.c. water  
 50 gr. pyrocatechol  
 50 gr. sodium sulphite ( $\text{Na}_2\text{SO}_3\text{Sicc}$ )
- B 500 c.c. water  
 30 gr. sodium hydroxide  
 50 gr. potass. bromide

Equal volumes of A and B are mixed a short time before use, as the mixture is unstable.

Development is complete in 20-35 seconds at  $18^\circ \text{C}$ . The film can be examined after partial fixation, which takes another two minutes in a rapid fixative. Such films fade, and cannot be preserved for record. This is not important, however, as two exposures are usually enough to position the ring.

So far as I am aware, the method has not been used in this country, though a less rapid method of development taking seven minutes and using hydroquinone instead of pyrocatechol has been employed by our orthopaedic surgeons, to localise the guides for Smith-Petersen pins in the femoral neck.

*The Lochfinder.*—The "Hole-finder" is a tiny "P. bulb" whose metal case bears a similar ring of hooks. This is moved about the sclera under (unlighted) ophthalmoscopic direction, until its glow coincides with a retinal tear.

*Objective determination of visual acuity.*—The visual acuity of children, illiterates, and malingerers, can be determined by measuring the maximum distance at which a moving test object provokes optico-kinetic nystagmus in the fixing eye.

A brightly illuminated white-painted strip is suspended from a spring, and oscillated in the vertical plane by a solenoid (Fig. 2). The strip is covered by fine black checks of a specific size, like a chessboard, and bears at its centre a strip of similar but larger check.

As the strip is seen through a slot which precludes a view of its edges, the normal eye has at 3 metres the impression of an immobile gray strip.

As soon as the patient is near enough to resolve the band of bolder check at the centre of the strip, his eye can be seen to follow it up and down.

Rieken based a night vision test on the same principle for the Wehrmacht, the patient being seated in the dark at a fixed distance from a revolving black drum painted with white strips.

The illumination of the drum was increased under photometric control until the conjunctival vessels near the outer fornix could be seen moving to and fro horizontally under a blue filtered ophthalmoscope light.

As misdirection of the light on to the pupil was liable to invalidate the test, Goldmann designed a contact lens with a clear centre

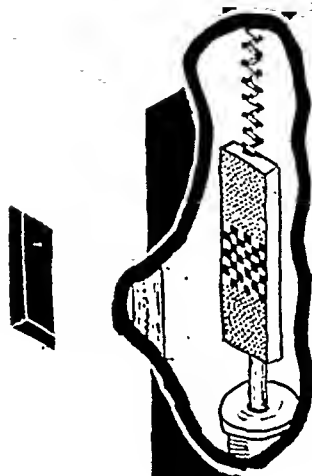


FIG. 2.

Objective determination of visual acuity (Goldmann). This is very diagrammatic, the length of chequered strip and the spring necessitating an instrument several feet high.

and eight spots of luminous paint on the blackened rim. These spots can be seen moving in the dark as soon as optico-kinetic nystagmus occurs in the wearer's eye (Fig. 3).



OBJECTIVE VISUAL TESTING  
RIEKEN—GOLDMANN

FIG. 3.

Night vision test.

*The auto-recording spherical perimeter.*—As H. M. Traquair, the leading British authority on this subject, has never ceased to point out, clinical perimetry is the most subjective form of examination in our speciality, the results are overlaid by the personal equation of examiner and examined, and it is the perimetrist not the perimeter that does the perimetry.

Goldmann, while admitting the force of this argument, holds that ultimately perimetry may become a science rather than an

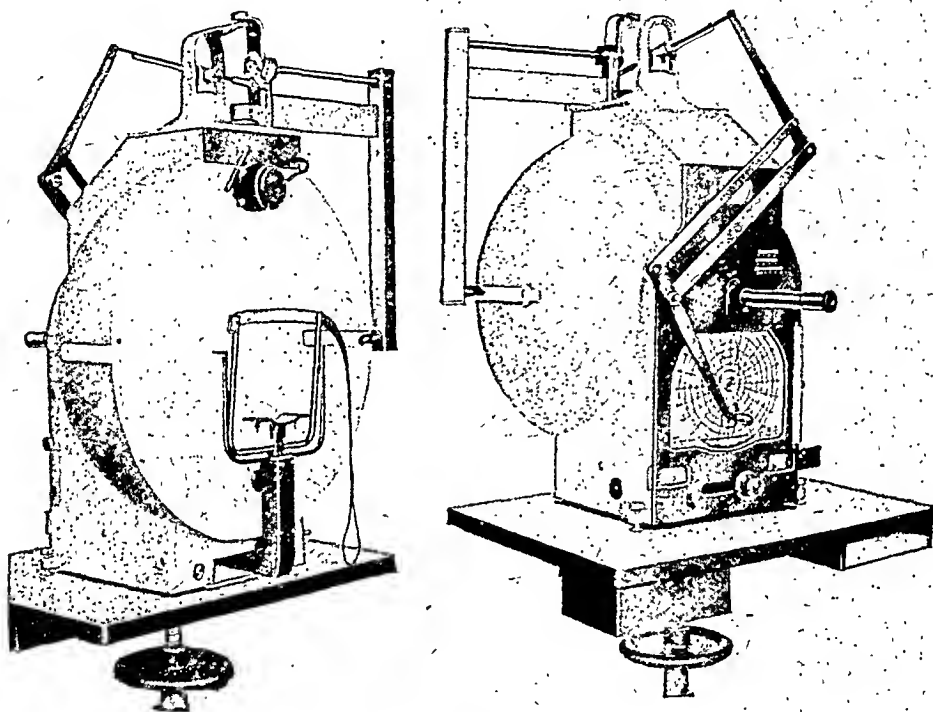


FIG. 4.

Goldmann's perimeter.

art, and that meanwhile it is possible to achieve a more standardised relative perimetry than is possible with existing instruments.

The perimeter designed to this end (Fig. 4) is the result of ten years of experiment and collaboration between Goldmann and Hans Papritz; the chief designer of Haag-Streit. I am much obliged to the latter firm for the loan of the blocks illustrating the device.

The test object is a spot of light (whose size can be varied by stops and the intensity can be controlled by filters) which is projected against a white hemispherical background whose luminosity is photometrically controlled.

As the area, luminosity, and sharpness of the edge determine the stimulus, the oval shape of the spot (Goldmann claims) is unimportant, but the speed of movement ( $5^{\circ}$  per sec.) contrast, adaptation, and background illumination (about 40 f.c.) are carefully standardised.

Fixation can be continuously controlled by the surgeon through a telescope, while the ingenious pantograph permits him to advance the test object at right angles to the margin of a scotoma, under fingertip control, and while watching the chart.

The telescopic opening is so small that it only prevents scotometric mapping of the field for  $1^{\circ}$  around fixation.

The isopters have been worked for objects of 0.25, 1, 4, and 16 square millimetres, employing different, specific filters, on thirty men between the 20th and 30th years, and another group between the 60th and 70th years.

It has been found that if the test object is enlarged four times, it will give the same peripheral isopters if its contrast with the background is reduced by 0.31. It has also been found advisable to correct refractive errors in testing the central isopters.

It was perhaps presumptuous on my part even to attempt to criticise so ingenious and beautiful a piece of machinery, but when I examined the pantograph at the clinic the highest joint between a cone and conical hollow looked rather fragile.

I later paid a visit to the Haag-Streit factory, which is like a private house in the country, at Liebefeld-Bern, about four miles away by bus. There the manager showed me I was quite wrong in thinking this joint could easily be put out of order. He took hold of it, and shook it vigorously enough to rock the whole instrument sideways without altering the adjustment in any way.

Two other minor criticisms are also possible. First, there is a small area on the horizontal meridian in each temporal field, in which recording is impossible. This corresponds with the nicks in each side of the hemisphere, and is not of importance.

Secondly, although the reflecting surface remains unaltered in the clear Swiss air, I suspect that the filthy atmosphere of industrial England would immediately alter its reflectivity.

Against this, Professor Goldmann tells me that the surface is washable, and that the isopters depend far more on changes in contrast, which can be standardised by the built-in photometer, than on changes in the overall brightness which is dependent on the age of the bulb and the reflectivity of the background.

All Swiss clinics give the place of honour to this perimeter, and have relegated that of Mäggli to second place.

Professor Goldmann also tells me that he has compared the instrument on the same cases with Pflüger's perimeter and the Bjerrum screen, and has found it superior to both of them.



The physiological value of the instrument is undoubted, and "a priori" one would expect it to be superior for clinical work to the perimeters employed here.

On the other hand, it costs £180, which as the Americans say "is not hay," and before purchase one would like to be assured by comparative tests on a series of cases that it will in practice indicate field changes of clinical importance earlier than, or has other advantages in diagnosis or prognosis over our own perimeters.

I might add that I have submitted all my notes and reprints to Mr. H. M. Traquair, of Edinburgh, who also holds this opinion.

*Binocular micro-gonioscopy.*—Both these techniques are based on the Haag-Streit (1937) slit-lamp on whose design Goldmann

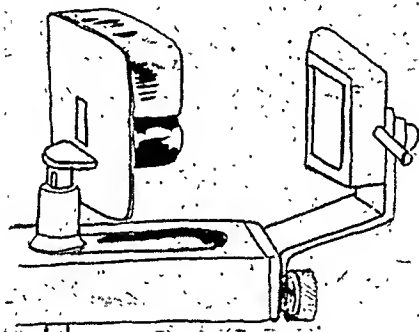


FIG. 5.

Goldmann's deviation prism fitted to Hamblin slit-lamp.

had considerable influence. I doubt if there exists a better lamp for clinical work.

As an excellent translation of Goldmann's description of the lamp and the two contact lenses is given in B.J.P.O. 1938 : 13 : 77, I will confine myself to features of practical importance.

The essential attachment for both techniques is a deviation prism which swings on an arm in front of the illuminating lens, and diverts the beam by internal reflection  $13^\circ$  right or left as required. This reduces the beam-microscope angle to  $5^\circ$ . This prism alone (on the Haag-Streit lamp) permits examination of the posterior vitreous without a contact lens. Fig. 5 shows an attachment to fix the prism to a Hamblin slit-lamp. I have insufficient data to comment on the effectiveness of this combination as yet.

The eye is anaesthetised by a warm 0.4 per cent. diocaine

(C.I.B.A.). This occupies a drop bottle in a thermostatically controlled heater, together with an undine containing normal saline, to fill the bowl of the contact lens. A practical British device of this type a "solution heater for two bottles" is made by Kelvin Lenses Ltd., Imperial Works, Allum Street, Manchester. Goldmann prefers diocaine as it has an almost instantaneous action.

When I tried to obtain it, C.I.B.A. informed me that "they withdrew diocaine many years ago, and advised nupercaine 1/100 as a substitute."

Nupercaine is stated to be as strong as 3 per cent. cocaine, but to act more quickly (30 secs.), and must be kept in alkali free glass. Unfortunately the 1/1000 solution recommended for ophthalmic use is only obtainable in England in ampoules which makes it too expensive for occasional instillation.

C.I.B.A. have kindly put up some nupercaine in drop bottles which I have employed for about nine months. The action resembles that of holocaine in "white eyes" though there is less initial irritation: corneal anaesthesia for tonometry and contact lens work is attained in one to one-and-a-half minutes and there is even less corneal disturbance.

Outside Berne, the Swiss have an expression, "Wie Ein Berner" meaning a "slow worker," so it is interesting to record that insertion and control of the contact lens, arrangement of the head on the chin rest, and focusing the lamp, requires a most un-Bernese degree of activity. The lens concavity is deep, and I find skilful handling is needed to prevent loss of saline.

The Haag-Streit lamp is a great help here, as the controls for

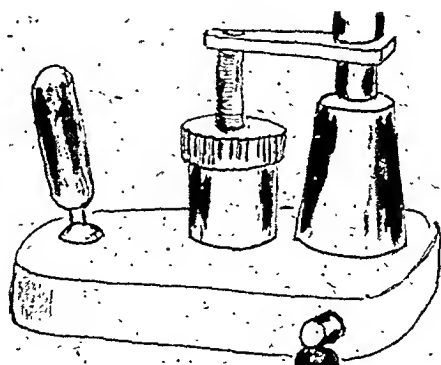


FIG. 6.

Controls of Haag-Streit slit-lamp (diagrammatic). The lever controls antero-posterior and lateral and the milled wheel the vertical movement of both lamp and microscope. (Note ball-bearing support of transverse element).

height, lateral and antero-posterior movements, are all in the compass of one hand (see Fig. 6), leaving the other free to tilt or rotate the contact lens as necessary, though it will often remain *in situ* without pressure.

I found later at the Haag-Streit factory that this lamp control is achieved by feather-light castings, and ball-bearing support of a transverse chassis element.

When you attempt these adjustments with the separated controls of an English lamp, you feel, like the Highlander who sat on an ant heap, that a third hand would be of great help.

As Busacca has indicated, the method has advantages over other methods of gonioscopy, which render it particularly suitable for clinical work. The patient is seated, an instrument in common

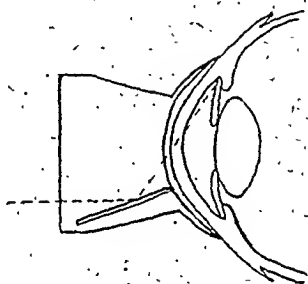


FIG. 7.

Goldmann gonioscopy lens. Dotted line represents path of incident and reflected light.

use provides  $\times 20$  binocular vision, and a narrow beam to estimate relief. By rotating the contact lens which contains a little mirror (Fig. 7) which both radiates the illumination in and reflects the image outwards, the whole angle is visible without moving the patient.

Incidentally, Busacca claims that the narrow beam shows the line of Schwalbe is not a prominence though to my untutored eye it appeared to be so in the cases I was shown.

The chief use of gonioscopy at Berne is to decide which glaucoma operation is indicated, and in which cases the post-operative result will be reasonably permanent.

For the narrow angles which accompany the shallow anterior chamber of congestive glaucoma, Goldmann advises iridectomy. A poor result is foreshadowed gonioscopically by visible remains of iris root or "nipping" of the lens edge in the incision.

Dieter's iridectomy (Fig. 8) overcomes both these difficulties, though if upward dislocation of the lens still occurs (as in malignant glaucoma) an intracapsular extraction is indicated.

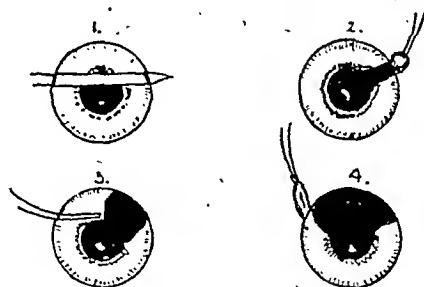


FIG. 8.

## Dieter's Iridectomy

While accepting that Dieter's method has special advantages, I have found personally that it is not too easy to perform. Unless the knife is entered rather high on the limbus, the iris is elastic, and the anterior chamber fairly deep, it is difficult to get a good grip and make the second iridectomy truly basal.

For the wide angles found in the deep anterior chambers of glaucoma simplex, cyclodialysis by a slight modification of Blaskovic's method is advised.

A radial incision of 3 mm. long starts 5 mm. from the limbus and the spatula inserted at right angles to the incision before being swept around.

The aim is a separation of  $\frac{1}{4}$  of the circumference and a good result is signalled by a permanent slit-like fistula occupying this proportion of the angle of the anterior chamber.

At this point one might conclude that the chamber depth was as good an operative indication as gonioscopy.

There is, however, a difficulty. Since 1938 certain cases of glaucoma simplex with deep anterior chambers have occurred with narrow angles.

Cyclodialysis in these cases was followed by acute glaucoma some days later.

In these cases, the cyclodialysis must be preceded by basal iridectomy *in the same quadrant three weeks earlier*.

It is clear both from our conversation and his "Kammerwinkel Studien beim Primärglaukom" (*Ophthalmologica*, p. 102, 1941), that Goldmann finds that the angle is narrow in acute and chronic congestive glaucoma.

During periods of high tension the angle may be closed over  $\frac{3}{4}$  of the circumference and during periods of normal tension, though open, it invariably remains narrow.

On the other hand, his observations differ from those of the American School, as he finds no sure and specific gonioscopic abnormality in most cases of glaucoma simplex.

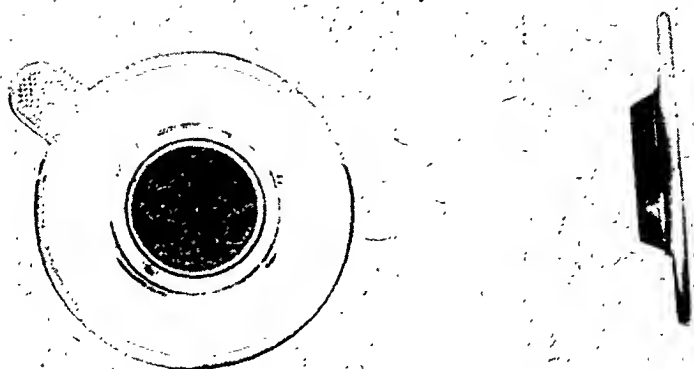


FIG. 9.

(Front view)

Hruby's lens for retinal biomicroscopy.

(Side view).

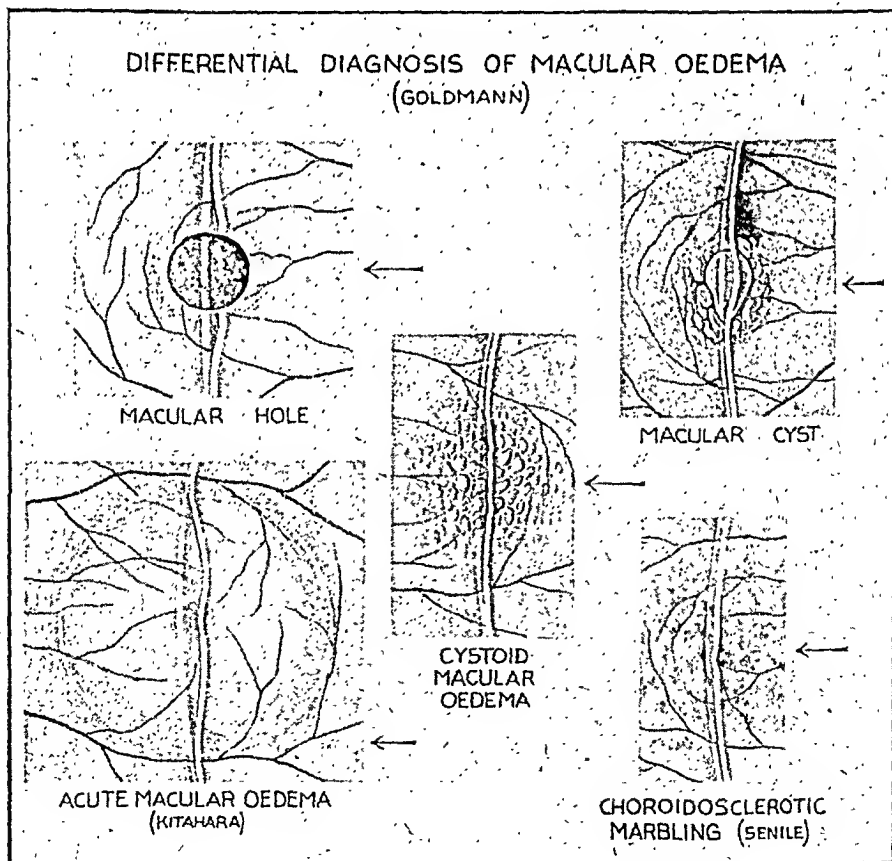


FIG. 10.

Biomicroscopy of the macula. (Drawing by Prof. Goldmann's assistant Iseli).

*Retinal biomicroscopy.*—The small flat-surfaced plastic contact lens (employed in conjunction with the deviation prism) resembles that of Koeppe, but has two lateral nicks which make it easier to handle. Sallman told me in 1936 that Zeiss were attempting to produce a lighter Koeppe lens with a plane face of 15 mm. diameter instead of the original 10 mm. Goldmann's lens appears to realise this ideal, as it has a plane face of 14 mm., only weighs 0.8 gramme; and remains *in situ* without being held. While not so simple as Hruby's method (Fig. 9) (a variant of that of Lemoine and Valois 1923, *vide* Lausanne) which does not require a contact lens, the optical results are superior when compared on the same case. It is difficult to get the Hruby lens really close to the eye in a trial frame.

Goldmann has developed a diagnostic technique for macular oedema, and the various possible appearances are shown in Fig. 10.

In a series of forty-two such cases, ten were due to senile choroidal sclerosis, and were improved by twelve retrobulbar injections of 0.4 c.c. of 0.1 per cent. atropine sulphate at three-day intervals.

Although the degree of improvement is unspecified, Goldmann regards this as a "useful" measure.

In 21 cases of the same series, the case was hypertensive, thrombotic or cyclitic, and treatment was ineffective. No attempt was made to treat macular "holes" unless a detachment occurred.

To save the visual field in two such cases, after a paralysing injection of novocaine into the muscle funnel, the patient was seated in front of the slit-lamp wearing the contact lens. A fine, needle-thin electrode insulated everywhere except at the tip was introduced through a scleral incision, and passed across the vitreous through the hole itself, and into the choroid, which was thus successfully diathermised under direct vision.

Other interesting techniques were mentioned, but not demonstrated in the course of conversation. For example, diathermy of small folds blocking the lacrymal canaliculi, and the introduction of rubber tubing into the tear duct itself at the end of a wire for chronic lacrymal obstruction (Bangerter's method). (*Ophthalmologica*, p. 107, 1944.)

The wire is first passed like a probe from above, grasped below the inferior turbinate, and drawn out of the anterior naris by forceps.

### Lausanne

This clinic is situated on a hillside with a beautiful view over Lac Léman. There are only 42 beds, but it looks larger than this, as it is joined to a blind people's home.

Though small, this school has been made famous by the work of Gonin on detachment, and a bronze plaque is erected to his memory in the Lecture Theatre. Gonin, Streiff told me, was the typical genius, dreamy in everyday things, and wrapped up in his work.

Professor Streiff, the present incumbent, comes of an ophthalmic family, his father being a pupil of Haab, later practised as an oculist in Geneva from 1905 to 1943. Streiff himself is a pupil of Franceschetti, and has all the wide surgical outlook of his teacher. He is particularly interested in lid plastics and keratoplasty. Our conversation was in French.

*Keratoplasty.*—He claims about 37 per cent. successes. He quotes Hata's ghastly case where glioma spread from donor to recipient (*Acta Soc. Ophthal. Jap.*, Vol. XLIII, p. 1763) for preferring a cadaveric donor.

While removing the remains of Descemet's membrane with fine curved "manicure" scissors, he protects the lens with a tiny silver "niblick." This instrument (invented by Arruga for protecting the lacrymal sac during dacrocysto-rhinostomy) was adapted by Franceschetti both for lens protection, and for separating synechiae during keratoplasty (Fig. 18b).

The 5 or 6 mm. grafts employed are always centred slightly to the inner side of the pupil. Their size obviates the necessity for pre-operative localisation of the pupil by transillumination.

Incidentally, Maurice Girardet, an oculist in Lausanne, unconnected with the clinic, has also invented several ingenious keratoplastic instruments. These include a ring for fixing the unexcised cadaveric eye while obtaining the graft (this avoids excision of the eye), deeply recurved scissors on a de Wecker mounting for removing Descemet remains, and a small "shovel" for transporting the graft itself. I am able to show the last, which he was kind enough to give me, and which I have found most useful in two cases since (Fig. 18c).

Girardet stresses that unfortunately the prognosis is best when the opacity in the recipient cornea is limited, and that grafts rarely remain clear when the corneal opacity is total. He has illustrated this point (*Jl. Suisse de Méd.*, Vol. XXII, p. 723, 1943) by beautiful colour photographs.

*Black light.*—Streiff employs "Black light" (ultra-violet) to localise dislocated lenses before, and capsular remains after, cataract extractions. I have been able to obtain the special bulb used (Typ. 57202/70 13 HPW Pilora 120 W. Philips), but have been unable to use it as "the screw lampholders are in short supply."

*X-ray localisation.*—Dufour, Streiff's assistant, has invented a

transparent protractor which can be applied to X-ray films taken of intra-ocular foreign bodies with a Goldmann's corneal ring (see Berne). This protractor (a) allows for the 10 per cent. distortion due to the spread of the rays, and (b) if the refraction is known or the corneal diameter estimated by keratometry for variations in size from the standard eye with refractive error.

"*Chenilles Processionales*."—I was unaware till shown photographs, that the caterpillars whose hairs cause such trouble in children's eyes, are processional, *i.e.*, form a long line one behind the other on a branch of the pityocampa pine. The French call them "Processionnaires des Pins."

*Retinal biomicroscopy*.—Hruby's method (*Klin. Monatsbl. f. Augenheilk.*, Vol. CVIII, p. 195, 1942) is employed to investigate "holes" in the disc and associated macular changes. This is a -55 O.D. (Busch) lens in a trial frame (Fig. 9), and with a diverted slit-lamp beam (Goldmann's prism) can be used for slit-lamp examination of the retina, without a contact lens. Streiff regards these changes as congenital, and was surprised to hear that a hole has been observed to follow a haemorrhage on the disc in England. Hruby's lenses are unobtainable in Switzerland, and this illustrated is a copy made to my measurements by Rayner & Co.

"*Jake*" toxæmia.—"Jake" (o-tri-cresyl phosphate poisoning) has been observed to cause papillomacular atrophy in a Lausanne French polisher, a point of interest in considering the effect of metabolic poisons on central vision.

On the other hand, it should be noted that Burley (*Jl. Amer. Med. Assoc.*, Vol. XCVIII, p. 298, 1932), describes temporal disc pallor and anaesthesia as signs differentiating disseminated sclerosis from this toxæmia when caused by ingestion of 2 per cent. of this poison in Jamaica ginger (Jake) extract.

A large group of such cases was recorded elsewhere in Switzerland when 200 soldiers on a route march developed paraplegia or peripheral neuritis from food accidentally cooked in machine gun anti-rust lubricant. That so many men ate the mixture is an extraordinary tribute either to the culinary qualities of Swiss machine grease, or to Swiss Army discipline.

*Tonoscopy or Ophthalmodynamometry*.—Streiff is very interested in tonoscopy, and in fact has produced a book about it, "*Der Retinale Blutdruck im gesunden und kranken Organismus*" (Wien, 1946). Some of the component pictures of Fig. 10 are reproduced by permission from this, and some from the Giroux-Guilbert Routit catalogue. This technique of estimating the retinal blood pressure may be used clinically by a few Britishers, but if so I have never heard one mention it, much less stress its value.

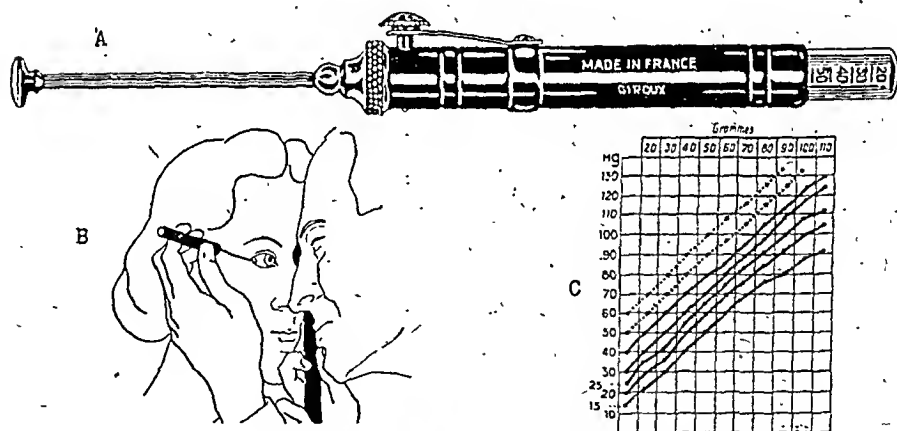


The instrument usually employed by Streiff and others abroad, is the "Ophthalmo-Dynamomètre du Docteur Baillart, à Bouton de serrage," No. 685 bis. Guilbert Routit et Cie (Fig. 11). This is a spring-loaded piston, with a rounded end, which is steadily pressed against the unanaesthetised conjunctiva overlying the insertion of the external rectus of a seated patient, until the arteries on the disc are seen by the ophthalmoscope to pulsate. Conjunctival cocainisation is only employed in the sensitive, and stress is laid on the site and steadiness of the pressure, an aim at the centre of the globe, and the tendency of the novice to get too high readings.

The button is then pressed to lock the instrument, and the pressure in grammes read on the scale by the light of the ophthalmoscope. This figure represents the diastolic pressure, and can be converted to mm. Hg by nomogram. The value is about 45 per cent. of the brachial diastolic when seated, i.e., with a normal intra-ocular and normal blood pressure 28 grams = 35 mm. Hg.

If the pressure is kept up till pulsation ceases, i.e. till the artery

#### OPHTHALMODYNAMOMETRY



- A. The Instrument. Makers: ~~Made~~ of Paris, showing locking button and scale reading.
- B. Mode of use according to Baillart, reproduced by permission of Professor Streiff, from "Der Retinale Blutdruck".
- C. Magitot-Baillart Nomogram. The tonometric tension is first measured by tonometer. The point of intersection of the oblique line starting from the tonometric figure and the vertical line which gives the dynamometer reading in grammes, gives the blood pressure in millimetres of mercury.

FIG. 11.

collapses, the scale reading is regarded as representing the retinal systolic pressure. Franceschetti regards this figure as less important than the diastolic, and Dubois-Poulsen does not take it in arteriosclerotics for fear of causing permanent damage.

Although certain German authorities hold that variability of the observational norm invalidates the method, Streiff claims that :—

(1) variations of  $\pm 10$  gm. from the norm indicate abnormalities of intracranial blood pressure after a head injury, and may explain unduly persistent post-concussive symptoms.

(2) posterior fossa tumours do, and anterior fossa tumours do not raise the retinal pressure relative to the systemic.

(3) that the prognosis of hypertensive retinopathy is worse if the retinal pressure is relatively higher than the systemic.

(4) that the visual and cerebral symptoms of the "carotid sinus syndrome" intermittent visual fog, vertigo, blackout, and syncope, occur because the retinal diastolic (hence by inference, cerebral) blood pressure falls disproportionately, by 40 per cent. when the brachial falls 10 per cent.

*The Carotid Sinus Syndrome.*—Tschermak discovered that light massage over the carotid sinus (clinically the point of maximum carotid pulsation) produced as a rule either bradycardia, or a fall of 10 per cent. in the systemic blood pressure or both.

Some individuals are rendered hypersensitive by local arteriosclerosis, cervical tumours, digitalis, or certain neurasthenic states.

These people may develop the symptoms described above, on extending the neck in a barber's or dentist's chair, or even on blowing hard at a fire.

One such patient was horribly burnt by falling on a fire he was blowing. It was found he could produce a syncopal attack by blowing hard against the back of his hand.

Curiously enough, Streiff has found that a hypersensitive sinus often occurs on the same side as retinal thrombosis, embolism or macular oedema, and believes they may be somehow related.

Thrombosis so caused might have analogies with the "Stagnation Thrombosis" (which B. A. Klein associates with a sudden drop in blood volume after head injury, operations, or early hypertension).

I have described this technique at greater length than some might feel justified, as I feel there must be many of the same generation in this country who like myself know nothing about it.

It is difficult also to overlook either its wide acceptance abroad, or that a continental jury in 1945 awarded Bailliart the quinquennial "Prix de Gonin" for his work on the subject.

## Geneva

Professor Franceschetti is already known to many Englishmen by his visits to the U.K. Congress.

A great deal of research has been carried out in this clinic, but its main interest to Englishmen will be the superlative surgery. The existence of other less well known clinics in the city explains the relatively small size (35 beds) which will shortly be increased by building to sixty, with a generous allowance of room for research laboratories.

*Genetics.*—In one laboratory I was shown the pedigree of the Glaser family, which has now been collected for thirty-five years, and covers four metres of paper.

Ludwig Glaser died in 1550 A.D. bequeathing severally to his descendants retinitis pigmentosa, retinitis punctata albescens, nerve deafness, and Friedreich's ataxia. Some inherited one, some more of these conditions, and Franceschetti believes a single defective gene is responsible for these varied defects.

*Ocular Myology.*—This is the only Swiss orthoptic department I saw which was fully equipped (with British instruments), and staffed by a wholtime orthoptist. There is such a department in Berne but I did not see it.

It is Franceschetti's interest in paralytic squint, however, which makes this clinic the centre of Swiss ocular myology, and prompts other clinics to refer difficult cases for diagnosis or treatment.

It seems to me that the vitality of the different national literatures on the treatment of ophthalmoplegia varies directly as the speed and efficiency of the test used to measure vertical deviation in the cardinal positions.

Duane's cover and parallax tests have obviously provided many American writers with a basis since the nineteen hundreds.

As the red and blue diplopia goggles, and Barlite, depend on the patient's powers of description, which are not always quick or accurate, and as the synoptophore only covers a limited zone of action, it was not until the 1930's that the extended use of the Hess co-ordimeter stimulated the British approach.

Franceschetti does not use Duane's test at all, and while not rejecting Hess's method entirely, has an approach based on four other devices of his own.

(1) *Franceschetti's Cyclophoromètre.*—The patient faces a tangent scale (known in Switzerland as the Croix de Maddox) at five metres, holding the cyclophorometer in front of one eye. In essentials this is a rotatable Maddox rod in a handle containing a spirit level (Fig. 12).

A trial frame is inadequate to hold the rod, as while the eyes fix the spotlight the head has to be strongly rotated to different



FIG. 12.

The cyclophoromètre of Franceschetti.



FIG. 13.

Testing of horizontal element in field of action of right inferior rectus and left superior oblique with "home-made" version of cyclophoromètre of Franceschetti.

angles (as suggested by Landolt), and tilted backwards or forwards.

In this way not only does the patient's statement of the relation of the red line to the scale figures establish the vertical and horizontal error in the cardinal positions, but by rotating the "rod" till it appears parallel (to him) with the horizontal arm of the scale he can indicate the varying cyclophoria at these angles.

A patient is shown holding a Leeds-made device of this type (Fig. 13) with the head angled to explore the action field of the right inferior rectus and left superior oblique.

I have found that even without the graduated protractor of the original device, the cyclophoria is much more obvious than the vertical error to a patient with a paralysed superior oblique.

I also find that one is apt to forget which quadrant is being tested, a difficulty that would be overcome, of course, by systematic use.

Franceschetti regards the following signs as of diagnostic importance:—

(a) the higher eye, the tilt of the false image, variation in diplopia with vertical movement, and "applied" lateral head tilt.

(b) vertical deviation with lateral movement, and unocular limitation of movement are regarded as less important, while:—

(c) "compensatory" head tilt and horizontal deviation in vertical diplopia are considered positively misleading. He underlines this last point in his schéma.

(2) *Franceschetti's "schéma."*—Most mnemonics flounder in an attempt to reconcile that the maximal vertical (diagnostic) action of a muscle is exercised in the opposite direction to its horizontal component.

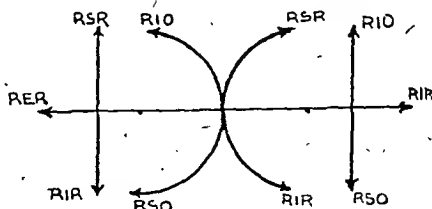


FIG. 14.

Franceschetti's schéma. "A mnemonic for the static and dynamic actions of the muscles of the right eye."

Franceschetti's schéma (Fig. 14) gets round this neatly by combining the "static" scheme of Marquez (which shows the action of the individual muscles from the primary position) with the "dynamic" scheme of Hess, which depicts the maximal vertical action in adduction or abduction.

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The combined diagram thus summarises the change in action with 30° lateral traverse from the primary position.

At these angles (although cycloduction may still be of importance), van der Hoeve has shown graphically that the horizontal component is negligible or actually reversed.

(3) *The double Maddox rod test.*—Even the Hess screen may fail to distinguish between paralysis of the superior oblique on one side and the superior rectus on the other, when secondary contracture of the antagonist has confused the issue.

A red Maddox rod is placed in one trial frame cell, and a white one in the other. Unless they are spring clipped, as in the "Oculus" trial frame, a piece of plasticine may be necessary to hold them both firmly. The head is then tilted to either shoulder, while the patient fixes a spotlight. If the head is tilted toward the shoulder on the same side as the affected eye, the red and white lines separate vertically, and vice versa.

This replaces the Hoffman-Bielschowsky apparatus which in any case few surgeons are likely to possess, and by establishing the side of the lesion at once clarifies the diagnosis.

(4) *The Franceschetti "Tableau."*—The signs of diagnostic importance (A) resulting from the tests described, are applied to the table shown (Fig. 15) to identify the weak muscle.

During my trip I found this table in use in clinics as far apart as Lausanne, Marseilles, and Paris.

Vertical Deviation	The Red Line and Transverse of Tangent Scale converge:—	Vertical Error Increased by Including Head to:—	Paralysed Muscle	Maximum Vertical Separation	Maximum Convergence of Images	Contracted Muscle	Maximum Vertical Deviation
RIGHT EYE HIGHER:	To Right (internal rotators)	to R.	R.S.O.	L. & down	R. & down	R.I.O.	L. & up
		to L. (often neg.)	L.S.R.	L. & up	R. & up	L.I.R.	L. & down
	To Left (external rotators)	to R.	L.I.O.	R. & up	L. & up	L.S.O.	R. & down
		to L. (often neg.)	R.I.R.	R. & down	L. & down	R.S.R.	R. & up
RIGHT EYE LOWER:	To Right (external rotators)	to L.	R.I.O.	L. & up	R. & up	R.S.O.	L. & down
		to R. (often neg.)	L.I.R.	L. & down	R. & down	L.S.R.	L. & up
	To Left (internal rotators)	to L.	L.S.O.	R. & down	L. & down	L.I.O.	R. & up
		to R. (often neg.)	R.S.R.	R. & up	L. & up	R.I.R.	R. & down

FIG. 15. FRANCESCHETTI'S "TABLEAU."



Cases when diagnosed are treated by prisms or surgery, as we do here. Cases of superior oblique paralysis have been operated upon successfully.

*Recurrent aphthous iritis.*—This is a recurrent hypopyon uveitis in young people, associated with oral aphthae or generalised erythema multiforme exudativum.

At the time of my visit this condition was scarcely mentioned in the English literature though it had been called Ophthalmitis Lenfa by Gilbert and Recidivierende Hypopyon Iritis in Germany. A good deal has appeared in the English medical papers since.

Known in Turkey as Behçet's (pronounced Bayshett's) disease, Behçet had actually sent a case to Franceschetti for a second opinion at this time, though in absence of aphthae it looked like any other iritis. The eight cases seen by Franceschetti were characterised by oral aphthae, recurrent hypopyon, complete resistance to all treatment, and ultimate blindness, sometimes from micro-cysts at the macula.

The possible relationship to bovine foot and mouth disease (though there are no nail lesions), and recurrent equine ophthalmia, is of great interest in view of past discoveries regarding brucellic uveitis, and Vail's recent work on the toxoplasma. I asked if sarcoidosis known there as the "Maladie de Besnier-Boeck" (pronounced Bayneeay-Book) might also have an animal vector, but was told "no."

*Corneal Grafts.*—Of the 110 corneal grafts done by Franceschetti in the last few years, 32 per cent. obtained a visual increase of 10 per cent., 14 per cent. were improved to 6/60, 34 per cent. retained the visual status quo, and 20 per cent. actually had worse vision post-operatively.

Franceschetti while recognising the existence of this last group (sometimes overlooked by other writers on this subject) regards it as no deterrent, as he is prepared to regraft such cases. With a normal anterior chamber the graft and bed are the same size, with a flattened cornea the graft is cut 0.1 mm. larger.

Large (5 or 6 mm.) trephines are employed, with an adjustable piston to prevent undue penetration (Fig. 16).

The piston fits so well that it requires a specially drilled vent to prevent air compression, and the edge (see section on Schaffhausen) is better than anything available here. The cost at present is rather high (about £12 a pair).

Franceschetti prefers trephines to knives, and believes the Americans have been driven to a knife technique by inferior instruments.

He regards the prognosis as good in disciform and interstitial keratitis, the apical scar of keratoconus, and heredo-familial dystrophy.

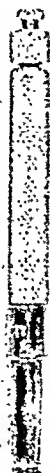


FIG. 16.

Franceschetti's trephine

I have been unable to trace a case history where the latter condition was grafted, and the graft invaded by the dystrophic process, but there seems to be a general belief in England and America that this always occurs.

Franceschetti disagrees, and produced as proof a farmer with Groenouw's type "B" dystrophy (see Fig. 20) grafted in 1935. This man had 6/9 and J.1 (uncorrected) in the better eye, and although the peripheral cornea was rough and the eyes irritable, there was no biomicroscopic evidence of invasion of the disc in either.

After I had examined him, the patient (obviously most grateful for the operative result) insisted on signing and giving me a little cyclostyled copy of his history. He had come to Geneva in 1935 to obtain a blind pension certificate, after four other hospitals had told him nothing more could be done.

Franceschetti has grafted thirteen similar eyes, and has employed the material to supplement Bückler's classification.

This successful approach stimulated me to base the table (Fig. 20) on facts from his papers, to show the constitution, location, depth and progress of the different types. Franceschetti was kind enough to correct it.

Recent senile cadaveric corneae are preferred, as the donor source, as he holds the graft to be merely a "scaffold," and the more inert the better.

The graft is stored up to seventy-two hours at 45° C. in holofusine (a sterile, pyrogen-free, isotonic Ringer type solution of essential blood salts, made by Haussman et Cie of St. Gall, but unobtainable here).

The solution is kept in a petri-dish and the graft is lowered into it on a small porcelain "strainer" with a central handle like an inverted mushroom. Fig. 17 which Professor Franceschetti kindly gave me.

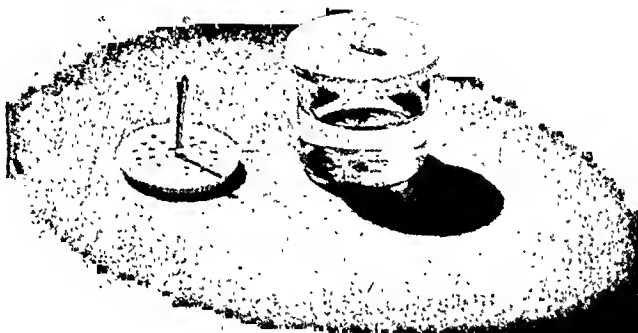


FIG. 17.

Corneal graft "strainer" Franceschetti.

As nothing of this shape is available here, and it is difficult to attach a handle to a porcelain filter disc, I got Thackrays to make a similar device out of chromium plated stainless steel.

Unless one has a "corneal bank" it is difficult to do a corneal graft just when one wants, so that Jean Nordmann "Chef de Clinique" at Strasbourg and myself had to wait until evening, when it was hoped a donor might become available.

The operation at 9 p.m. was a re-graft on a young man with interstitial keratitis, and 6/12 in the other eye.

A willingness to graft a bad eye when the other has good vision is, I feel, the acid test of a surgeon's belief in his technique.

Franceschetti, when operating, uses sterile linen gloves, retrobulbar anaesthesia, Arruga's speculum, scalytic lighting, and broad-toothed fixation forceps. A drop of pilocarpine is inserted half-an-hour before operation.

Four marks are made on the limbus at 12, 3, 6 and 9 o'clock, with methyl violet, and double armed sutures are inserted at these points.

Franceschetti's trephine (Fig. 16) cuts a very clean disc, and a thin remaining strand of Descemet's membrane was easily divided by Elschnig's "Hornhautmesser" (Fig. 18a) while the opaque

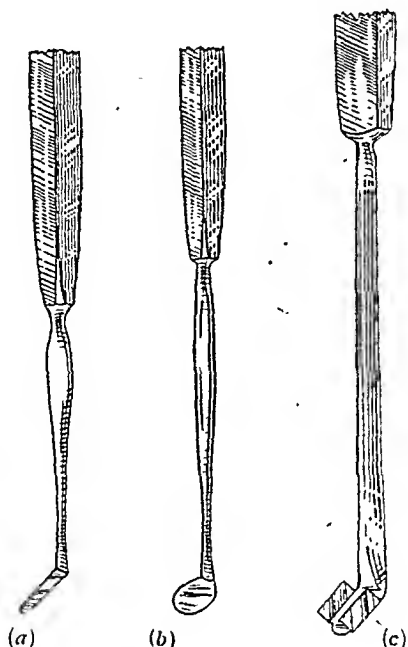


FIG. 18.

- (a) Elschnig's "hornhautmesser."
- (b) Franceschetti's "niblick."
- (c) The "pelle" of Girardet.

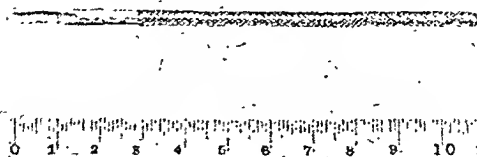


FIG. 19.

Franceschetti's gouge for removing Descemet remains.

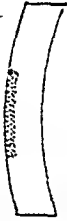



disc was held in forceps, and the lens was protected by the little "niblick"-shaped silver spatula held by an assistant (Fig. 18b).

This instrument is then swept round the anterior chamber to detach any synechiae.

FIG. 20.—*Familial Corneal Dystrophies*

Histology — Franceschetti

Classification — Bücklers

TYPE	APPEARANCE	SITE	ONSET	VISION	HEREDITY	HISTOLOGY
GROENOUW (A)	"CRUMB"		10	VARIOUS (3 cases)	DOMINANT	HYALINE DEGEN. OF BOWMAN'S MEMBRANE, SUB- EPITHELIAL BASOPHIL GRANULES.
HAAB- DIMMER	"LATTICE,"		16	BAD AT 50 (1 case)	DOMINANT	AS ABOVE BUT COARSER AND INVOLVING DEEPER LAYERS ALSO.
GROENOUW (B)	"SPOT"		1-10	VERY BAD (4 cases)	RECESSIVE	AS ABOVE + AN ALBUMINOUS DEPOSIT IN ALL CELLS OF THE CORNEA.
HURLER	+ OR — GARGOYLISM		BIRTH	MODERATELY GOOD STATIONARY. OFTEN UNILATERAL.	RECESSIVE	DISSOCIATION OF LAYERS. LIPOID GRANULES IN THE CONNECT- IVE TISSUE.

The Hornhautmesser (Augenärztliche Operationslehre 1922 : 525 : Fig. 447) is an angled knife, with a blunt point and two lateral edges. The English reproduction (Fig. 18a) is by Down Bros.

Had any ungraspable Descemet tags remained attached to the edge of the trephine bed, they would have been divided against the "niblick" by a tiny gouge-shaped instrument (Franceschetti's) equivalent to about  $\frac{1}{8}$  of the diameter of a 5mm. corneal trephine (Fig. 19).

Strands of Descemet's membrane rarely remain attached to the graft itself, but if they do highly curved scissors are to be preferred to the instruments above, as the pressure or traction necessary for their use might damage it. Though the cutting action of instruments for removing these strands varies greatly it should be noted that the most successful have a common feature—a curved cutting edge concentric with or of smaller arc than the trephine hole.

The graft was lifted out of the holofusine on its little "strainer," pushed on to the back of a metal lid spatula repositor, and from there to its bed by an iris repositor. The sutures were tied, argyrol inserted and the eyes double-padded. Time about 25 minutes.

Among the instruments in reserve were Arruga's forceps, which can be employed to put sutures directly through the graft edge at two points if there is a vitreous loss.

It is difficult to convey in a bald account of the technique the smoothness and absolute confidence of the whole procedure.

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## RETINAL ARTERY OCCLUSION

### A Report Illustrating the Pathogenesis of the Fundal Appearances and the effect of Acetyl-choline\*

BY

I. C. MICHAELSON

GLASGOW

THE following case is described because it illustrates:—

- (1). The rôle of spasm in arterial occlusion and the effect of acetyl-choline;
- (2). A relationship between arterial spasm and anatomical changes in the vessel wall;
- (3). The nature of the retinal opacity with the influence of the capillary distribution in determining its extent.

---

\* Received for publication, August 9, 1947.

The female patient, aged 41 years, was first examined on April 22, 1947. She then stated that the vision of the left eye had been defective since April 16 and that she had had headaches for several days following the onset of the visual defect. The vision of the left eye had previously been as good as that of the right.

On examination the right eye was found to be normal and to have a visual acuity of 6/9 with +4.50 D. sph. +1.50 D. cyl. 90°. The retinal vessels were free from any abnormality. The vision of the left eye was reduced to counting of fingers at about one metre. The pupil was slightly larger than that of the right eye, but reacted to light. The media were clear but the fundus showed a large triangular area of white opacity in the retina situated in relationship to the macular branch of the inferior temporal artery, as indicated in Fig. 1. The junction of the inferior temporal artery and its macular branch was obscured by a bright linear reflex. The white retinal opacity was very sharply defined below and above by the inferior temporal vein and its macular branch respectively. One very striking feature was that the affected branch of the inferior temporal artery was venous in colour where it became discernable beyond the retinal opacity. The rest of the fundus was normal and the retinal vessels showed no unusual features.

The diagnosis of occlusion of the macular branch of the inferior temporal artery was made and the patient was admitted to hospital. At 7.45 p.m. that evening the condition of the fundus remained as already noted and 0.1 gm. of acetyl-choline was injected retrobulbarly, atropine having been previously instilled into the eye. Fifteen minutes following injection the white opacity in the retina was noted to be markedly diminished and to be confined almost entirely to the area between the affected artery and macular vein. One hour later the condition was very much the same. The following day there was noticed no further change in the retinal opacity but the occluded artery at its junction with the inferior temporal artery could be seen for first time. It had a well developed central light streak. Fig. 2 shows the appearance of the fundus on the day following treatment with acetyl-choline. During the next few days the retinal opacity disappeared completely. Thirteen days after the onset of the occlusion and seven days after its relief with acetyl-choline a faint sheathing was noticed for the first time at the site of the spasm. It gradually became more apparent and Fig. 3 indicates its appearance on June 5. There was little visual improvement to parallel the ophthalmoscopic changes, but when last examined she could see the lower part of the letters of 6/24 line on Snellen's chart with +4.50 D. sph. and +1.0 D. cyl. There was no peripheral field defect using a 2/300 white object but there was a loss of the upper field to a 2/2000 white object on the Bjerrum

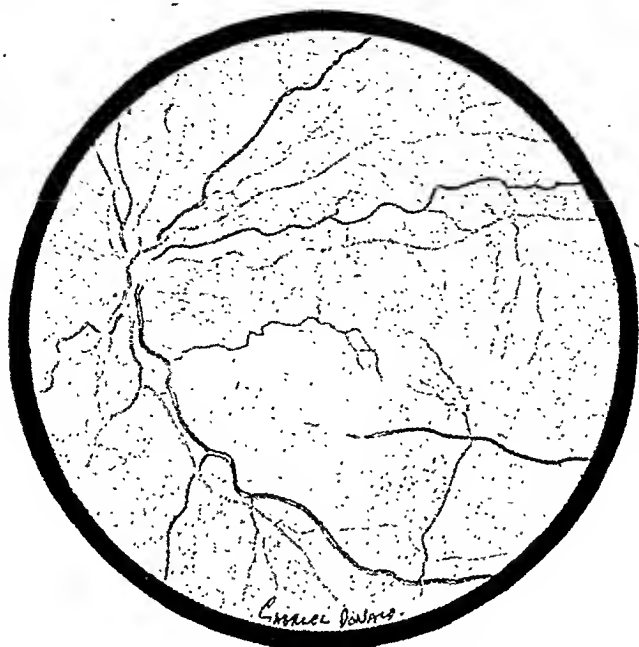


FIG. 1.

Appearance of fundus on April 22, 1947, showing the area of white retinal opacity sharply defined below by the inferior temporal vein and above by its macular branch.

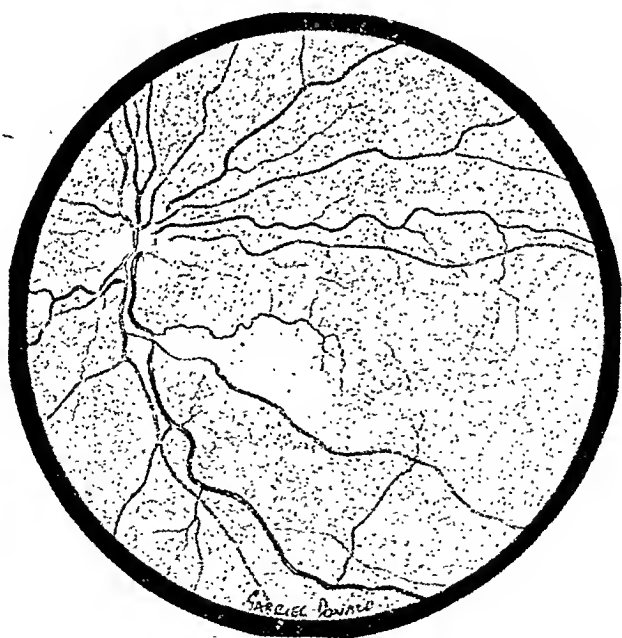
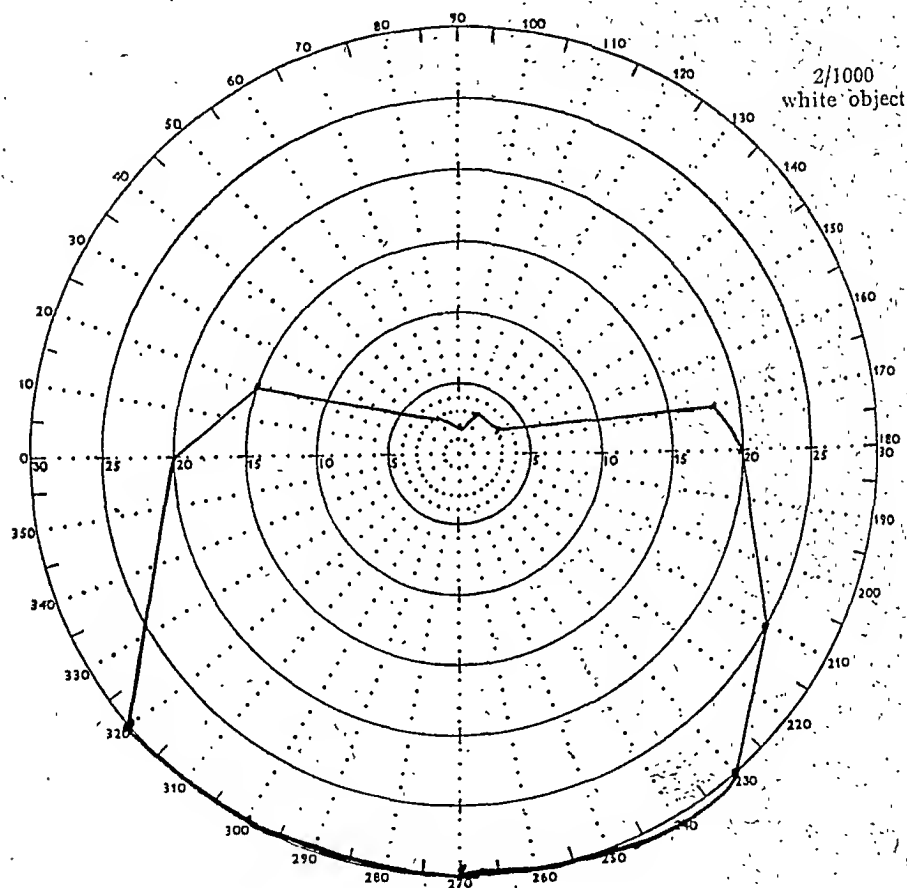


FIG. 2.

Appearance of fundus on day following treatment. The area of opacity is markedly diminished and confined almost entirely to area between affected artery and the macular vein. Note that the affected artery has now resumed its arterial colour.



screen (see chart). A general examination was carried out by Dr. L. Scott. The blood pressure was found to be 120 mm. Hg systolic and 70 mm. Hg diastolic. Apart from a low haemoglobin estimate (64 per cent.) no abnormality was found. She gave an indefinite history of headaches which, however, do not appear to have been of the migrainous type.



Since Raynaud's observations in 1874, angiospasm has been repeatedly observed to be the cause of arterial occlusion in the retina. Apart from the elderly with hypertension and arterio-sclerosis the condition occurs in young or middle-aged individuals who may show other evidences of vascular irritability such as epilepsy or migraine, or in whom may be present vascular sensitivity to various factors, such as toxins from influenza, malaria, or pregnancy (Mylius 1928, Sedan 1929, Griffith 1931, Davenport 1931, Freeman 1933, Selinger 1937, and Schousboe 1937).

Arterial angiospasm may occur in young people who otherwise

have no evidence of vascular irritability. (Ormond 1918, Traquair 1933).

The present case belongs to this last group. The localised sheathing was not present until the seventh day following the relief of the spasm and its development to the stage noted in Fig. 3 was reached 43 days after the onset of the occlusion. The spasm had apparently occasioned the sheathing which, with the local narrowing of the blood column, probably indicates intimal proliferation and degeneration (Ballantyne, Michaelson, and Heggie 1938). The vessel wall spasm-proliferation relationship shown in this case is of

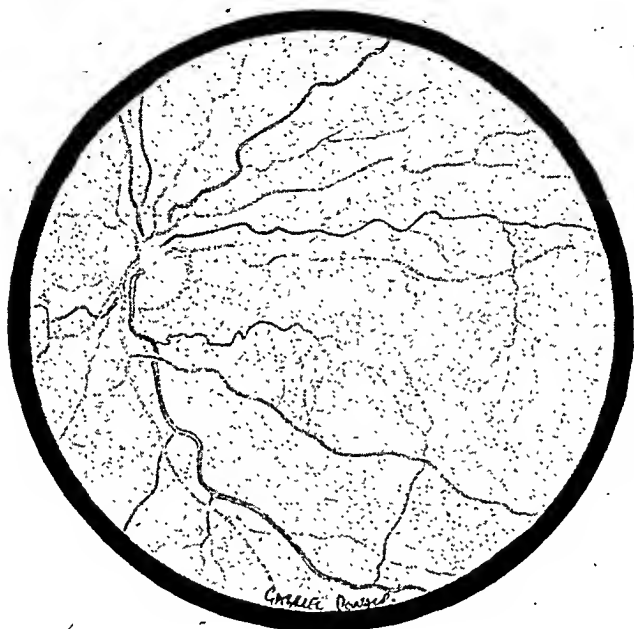


FIG. 3.

Appearance of fundus 43 days after onset of occlusion. At the site of spasm there is well-marked parallel sheathing of the vessel.

interest because it possibly illustrates in miniature a course of events, less acute but more diffuse, which may occur during the evolution of the general vascular changes of hypertension.

The beneficial effect of acetyl-choline on arterial occlusion due to spasm has already been noted by several observers. There is little doubt that acetyl-choline in this case relieved the spasm and restored the circulation. It is of interest there was no notable change in the diameter of the other retinal vessels following the injection, although search was repeatedly made. This lack of general response in the retinal vessels has been noted in two other patients treated with this drug. The localised effect of the drug on the spastic portion of one

vessel in the fundus and the absence of response by healthy retinal vessels appear to invalidate any conclusions regarding the efficacy of acetyl-choline in spastic occlusion which may be made from the negative findings of experiments on animals which have normal retinal arteries.



FIG. 4.

Portion of an injected human retina with artery above and vein below, selected as representing the triangular area of the capillary bed lying between the affected artery and the inferior temporal vein in the case described and because here likewise the ultimate arterial divisions (A) do not cross the vein.

The rapid disappearance of the white opacity suggests that it was due to oedema consequent on capillary stasis and anoxaemia resulting from diminished arterial inflow. Dunn (1940) has noted "that where an arterial supply is abnormally narrowed but not completely cut off, blood still passes to the vessel's natural territory under pressure at a less minute volume, and capillary engorgement in the area may be determined by this flow from the narrowed vessel itself even if there are no collateral anastomoses." During the

period of spasm the affected artery beyond the occlusion was filled to its normal width with venous blood (Fig. 1), and it would seem that de-oxygenated blood in the dilated capillary plexuses has found it possible to pass into the artery "below" the constriction because of the diminished pressure within it. The artery is occluded at a place where it crosses a fork formed by two veins and, as can be seen from Fig. 3, no branch from the affected vessel crosses either of these veins. Fig. 4 from an injected human retina illustrates the manner by which under these circumstances, the capillary territory served by the artery is limited by the neighbouring vein; and in the case under consideration the constituent veins of the fork. As a consequence the oedema arising from the capillary disturbance is exactly limited by the veins above and below the artery as illustrated in Fig. 1.

### Summary

- (1). A case of retinal arterial occlusion is described in which the cause was arterial spasm.
- (2). The spasm continued for 6 days and was overcome with acetyl-choline.
- (3). Localised sheathing of the vessel wall resulted from the spasm and was detected 13 days after the onset of occlusion.
- (4). Acetyl-choline does not appear to affect noticeably the diameter of healthy retinal vessels in man.
- (5). The white retinal opacity was due to oedema.
- (6). The disposition of retinal capillaries determined the extent of the retinal opacity.

I am indebted to Mr. Gabriel Donald for his care with the illustrations.

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## ANNOTATION

## Be sparing in praising and more so in blaming

The title of this month's annotation is taken from the Fourteenth Century allegory, the vision of Piers Plowman, A.D. 1362. The actual wording often varies. Benham's Dictionary of Quotations gives it as above and adds a Latin edition, *parum lauda, vitupera parcius*; but does not tell us from what author it is taken. Maybe it will be found in some early father of the church or perhaps in monkish Latin. We do not think it occurs in the Vulgate. Cicero's *parcius dicere de laude alicujus* gives the essence of the first part of the proverb, but he does not appear to have included the blame.

When dealing with praise or blame we are reminded of the old instruction to the novice when performing tracheotomy; keep in the middle line. Animate and inanimate matter are comprehended in the question. For instance we can blame or praise a person or persons or a thing or things. Into the last category comes the reviewing of books. You can praise or blame yourself and others can do it for you. Self-praise is always most obnoxious and we have Sterne's authority for saying that Dr. Joseph Hall, Bishop of Exeter, in the year 1610 gave his opinion "that it is an abominable thing for a man to commend himself." At public gatherings and in proposing healths Sir Anderson Critchett once laid down a sound rule of conduct when he said in proposing a health that he always tried to remember that his business in so doing was to toast and not to butter.

No one can object to a modicum of praise when a health is being proposed, but too much laudation makes the victim feel uncomfortable. Even Samuel Johnson, who, it is said by a strange slip in proof reading, once figured on the printed page as the great *Chum* of Literature, got tired of the persistent flattery administered in his presence by an eminent literary lady and told her to stop it. She has been identified in the notes as probably Miss Hannah More.

In book reviewing it is just as well to be tolerant and not to praise or blame too freely. No book is so bad but that some good thing can be found in it is a maxim as old as Pliny. Manifest errors are fair game, but on debateable points we should not blame an author because we happen to disagree with him. Heterodox opinions do sometimes get into print. Occasionally they are due to faulty proof correcting. This is perhaps not so likely to occur in an ophthalmological treatise as, shall we say, in a list of historical dates. Suppose a case in which the date of the Black Death of 1348/49 gets entered by an error as 1548/49. We are then two hundred years out. We all know how very easy it is to pass a

"five" for a "three" unless we have all our wits about us. Should such a slip occur we prefer to look upon it as a slip and not ascribe it to ignorance.

In dealing with patients, it is a truism to say, as we have observed on previous occasions, that they sometimes invert the sequence and blame us for things we could not help and, more rarely perhaps, praise us for some result when we know in our heart of hearts that we have deserved blame rather than praise. Say what you like, no one objects to praise in moderation. Blame is not so easy for us to be satisfied with; but there is one occasion in which the person blamed may derive an unholy gusto, and that is when he can prove the blamer to be wrong. A very early experience of the writer's was of this nature. We had just come into residence as house surgeon and had to assist one of the assistant surgeons who was not normally attached to our firm. The operation was that of complete removal of the breast. We were subjected to a running fire of caustic criticism until, about a third of the way through, we were asked why in heaven's name we did not put a clip on that vessel. The vessel in question was the intercosto-humeral nerve and we protested that an artery forceps there was out of place. The rest of the operation was completed in silence, and we thanked God that he had allowed us to remember this elementary anatomical point.

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## THE OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA (British Medical Association)

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### Annual Meeting

THE seventh annual general and scientific meeting of the Ophthalmological Society of Australia (British Medical Association) was held at the Royal Australasian College of Physicians, Macquarie Street, Sydney, on September 23, 1947. Dr. Darcy A. Williams, the President, in the chair. Those present included three members from Queensland, thirty-seven from New South Wales, thirteen from Victoria, two from Tasmania, four from South Australia and one from Western Australia.

### President's address

The President, Dr. Darcy A. Williams, after welcoming such guests as had been able to attend, addressed members upon the subject of early ophthalmologists in Australasia and upon the associations of ophthalmologists with Australasian medical congresses. Amongst the early ophthalmologists mentioned by the

President were James T. Rudall, Andrew S. Gray, T. Aubrey Bowen, Charles Gosse, Thomas Evans and W. Odillo Maher.

The gradual growth of ophthalmology was traced and the manner in which it kept pace with changes overseas was described. An endeavour was made to salvage from the past valuable material and interesting and at times amusing anecdotes.

### Research technique and training overseas

N. M. Macindoe (Sydney) who had recently returned from a visit to Europe and the U.S.A. where he had made close enquiries into subjects of ophthalmological interest, read two papers, accompanied by fifty illustrations, showing recent advances in research and technique, and trends in organisation and training abroad. At Boston research was concerned with the subject of steamy cornea, optic neuritis and the visual acuity of moving objects; at Johns Hopkins with virus diseases and sympathetic ophthalmia; at New York with colour vision; at London with parietic strabismus; at Copenhagen with colloidometry; and at Stockholm with chromatic light and electro-retinograms. At Zurich work was being done on corneal distortion, subjective screens for central scotomata, perimetry, slit-lamp examination of the fundus, the content of the pathological aqueous, tonometry and ciliary permeability. New technique described included gonioscopy, drug treatments, radio-active iodine, scleral resection in myopia, corneal grafting, glaucoma, cataract and retinal detachment operations.

The section on training was a reasoned appeal for more apprenticeship and fewer academic examinations. The continental clinic system was described and the suggestion put forward that we copy the American type of organisation in our big centres.

### An outline of orthoptics in New South Wales

Miss E. Russell read a composite paper expressing the general opinion and experience of five senior practising orthoptists. The practice of orthoptics by orthoptists began in Sydney in 1933. At the present time eleven orthoptists were working in hospitals, intermediate clinics and private practice, and an average of 576 treatments were given each week.

In the early years, squint formed the great majority of cases, prisms being used for phorias as a general means of relieving or attempting to relieve symptoms. While the treatment of strabismus went on in growing numbers, the realisation of the great benefit orthoptic treatment was to phorias and their allied types had widened this field amazingly. Phorias of all types were receiving increasing attention since these were the cases where distress might

be acute. Orthoptists felt that their greatest battle was still with strabismus and it was there that they did their toughest job. They had learnt during the years to assess the relative possibilities of success with the different types. With all types suppression was their greatest enemy.

As regards convergent squints, true accommodative cases responded to treatment only and borderline squints needed surgical help. Tonic squints required orthoptics before and after surgery. Congenital cases were often successfully treated.

The treatment of divergent squint was less difficult. With all cases of strabismus orthoptic investigation was important before surgery to assess the binocular condition, *i.e.*, abnormal projection, etc. Suppression was their greatest enemy. Occlusion was their greatest ally. Treatment had been speeded up generally. There would always be cases, difficult in themselves, and rendered more so by mental dullness, inability to concentrate, frail health and indifferent parental co-operation, where treatment would be lengthy which eventually could be cured or greatly improved. As long as definite progress was being made they felt treatment should continue.

#### The selection of patients for orthoptics: some remarks:—

John Antill Pockley. Sydney

Some factors in the selection of cases for orthoptics were indicated. It was concluded that the personality of the patient and parent was of first importance in the selection of many cases and that in adults many phorias arose from psychogenic causes. It was desirable to aim at the earliest possible cure and when conditions were suitable operation should be early. Waiting for your children to reach orthoptic age was undesirable. A close liason between ophthalmic surgeon and orthoptist was essential.

#### Two cases of choroidal melanomata with unusual histories

Dr. Kevin O'Day (Melbourne) read a paper on two cases of intra-ocular tumours of unusual interest.

The first was a malignant melanoma of the choroid. Four years before the eye was finally removed, the patient had been advised by four ophthalmic surgeons that removal was necessary because of a malignant tumour. Even after four years the tumour was not very large. The eye was slightly inflamed, but there was no evidence of glaucoma. Very little pigment was present in the tumour. There was a metastatic nodule at the root of the iris. The tumour was of mixed-celled type with many thin-walled blood sinuses. Mitotic figures were very difficult to demonstrate. Wilder's stain demonstrated dense reticulin in the base of the tumour, with very little at



the summit where it had broken through Bruch's membrane. Wilder was of the opinion that the prognosis was better in tumours with a dense reticulin. The speaker suggested that this stain should be done on every case in which the eye was excised because of its probable prognostic significance.

The second case was a retino-blastoma in a man aged 29 years, an unusual age for this tumour. The patient gave a history of loss of vision, and pain in the eye after an injury at football. When first seen the vision was reduced to hand movements in the temporal field. The tension was raised and the anterior chamber full of blood. After cyclodialysis the pain and the tension were relieved and the man went back to the country. He returned a year later with the history of a further blow at football, and the eye completely blind and painful. The tension was raised and the eye-ball enlarged with a ciliary staphyloma on the temporal side. The anterior chamber was full of blood. The eye was excised. When it was opened, the tumour was found to involve the retina, the iris, ciliary body and the anterior chamber. A cyclitic membrane was present, and the tumour cells were growing along this. A portion in the ciliary body was anaplastic, but sections of the retina demonstrated the mantles of cells surrounding vessels, typical of retino-blastoma. Actively growing areas alternated with necrotic ones. There was no evidence of extra-ocular extension, although mitotic figures were very numerous.

### The treatment of dendritic ulcer

Dr. Frank Phillips (Hobart) described his treatment for dendritic ulcer, which included removal of the damaged tissue with blotting paper and the use of a dental drill on the more resistant areas of ulceration. He maintained that his treatment was better than the customary methods.

### Endothelial dystrophy

Dr. Clifford S. Colvin (New South Wales) described a case of endothelial dystrophy in a female patient aged 62 years. The case showed improvement after glandular and vitamin therapy. Dr. Colvin concluded his paper with an illuminating discussion on this uncommon and interesting condition.

### Dry Eyes—a further contribution to their study

Dr. J. Bruce Hamilton (Hobart) gave a paper on the subject of kerato-conjunctivitis sicca, amplifying his paper read before the Society in 1940 (Transactions, Vol. XI). He reported another 24 cases and described their treatment, which had generally satisfactory

results. Dr. Hamilton discussed the differential diagnosis of the condition and its relation to Mikulicz's disease, Plummer-Vinson syndrome and iodide mumps.

He pointed out that the disease was of great interest in its possible association with other common morbid processes.

### Allergic sensitivity to procaine hydrochloride and the hypodermic injection of cocaine hydrochloride—a personal experience

Dr. Arthur D'Ombrain (Sydney) dealt with the characteristics of drug allergy and he gave a harrowing personal experience of dermatitis due to procaine. He maintained that collapse from cocaine injection was really an outright poisoning and not an anaphylactic reaction. He related personal experience in the use by injection of 0.75 per cent. cocaine hydrochloride, over a period of six years. Dr. D'Ombrain's opinion was that cocaine could be injected with safety, provided a correct concentration and dosage were used.

### Eye protection in industry

Dr. A. L. Tostevin (Adelaide) stressed the necessity for greater co-operation between oculists, industrialists, lighting engineers, architects, the Nation Safety Council and the Standards Association in regard to, not only the protection of eyes in industry, but also in the field of sight testing and correction of vision of employees.

Examples of eye injuries in the various large industries were given and reference was made to the I.C.A. Safety Council as a guide to industry towards protecting the worker and improving his efficiency. Emphasis was placed on the fact that most of the metal industries showed that 50 per cent. of the lost time from accidents was due to eye injuries.

Dr. Tostevin surveyed the research work being carried out in Australia and also the measures to be taken in prevention of eye injuries generally.

### A Case of partial thrombosis of the central retinal vein treated by dicoumarin

Dr. R. G. Banks-Smith (New South Wales) gave extracts from available literature on this subject. The types of this condition were described and indication was given of those types in which treatment might be successful.

Dr. Banks-Smith submitted a case report in which partial success was claimed and he issued a warning as to the possibilities of over-dosage.

### Radon treatment of intra-ocular tumour

Dr. W. Lockhart Gibson (Brisbane) sketched a short history of the various methods of radiation that had been used, and drew attention to the value of active co-operation of the biophysicists with the radiotherapists in working out accurate dosage. He described the use of a radon seed bent into the form of a circle with a spoke in it and moulded to the curve of the globe of the eye. Dr. Gibson claimed that such a seed was easy to suture in position, and could be arranged to give an accurate dosage to the tumour and as little radiation as possible to those parts of the eye which were so extremely sensitive to radiation.

Charts of isodosage were exhibited and the treatment of a child with two tumours in its only eye was described.

### The Lagrange operation—a summary of sixty cases

Dr. J. A. O'Brien (Melbourne) presented a summary of sixty cases of Lagrange operation for glaucoma. He explained various modifications of technique. His results with complete or button-hole iridectomy were similar and his percentage of successful operations totalled eighty-five.

### A preliminary survey of ophthalmic diseases in Western New South Wales

Dr. K. B. Redmond (New South Wales) analysed two thousand case records of patients in Western New South Wales, taking into account the geographical area of residence and environmental conditions of life and work. The areas included part of centre tablelands, the central western slope and the western plains. He concluded that factors of sunshine, dryness, glare and dust were important. He presented a table of ophthalmic diseases and their percentage incidence.

### Non-magnetic metallic intra-ocular foreign body

Dr. Lennox Price (Newcastle) said that in civil practice it was unusual to meet a case of penetrating wound of the eye with a retained intra-ocular foreign body which was metallic and yet non-magnetic. Under war conditions, on the other hand, such cases occurred more commonly.

Reports were given of two cases of this type which were treated within a few weeks of each other. The histories, clinical features and results in each case were compared and contrasted.

### Optic neuritis following measles

Dr. T. C. Meurer (New South Wales) dealt with optic neuritis and post-neuritic optic atrophy following measles. He said that the condition was a result of an encephalomyelitis which occurred late in the course of measles usually when the rash was beginning to fade. The resulting optic atrophy did not appear to have any relation to the severity of the encephalomyelitis or the severity of the attack of measles. Three cases were reported and a review of the literature presented.

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### Social

The annual dinner was held at the Royal Automobile Club of Australia and was attended by forty-two members and guests.

On the evening of the opening day a cocktail party was given at the Wentworth Hotel by the Ophthalmological Society of New South Wales to members and their ladies.

The President offered the congratulations of the Society to Dr. J. Bruce Hamilton who had been appointed President of the Section of Ophthalmology of the British Medical Association Congress, Sixth Session, Perth.

Dr. Hamilton was also congratulated on his election as President of the British Medical Association, Tasmanian Branch.

### Annual General Meeting

The annual general meeting dealt with general business. Dr. Claudé Morlet was elected President for the ensuing year, and Dr. Arthur H. Joyce, Vice-President.

It is proposed to hold the eighth annual general and scientific meeting at Perth in conjunction with the British Medical Association Congress Sixth Session, August 15 to 21, 1948.

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## CORRESPONDENCE

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### COLOUR VISION IN THE CONSULTING ROOM

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—It is not important to argue further on the differing incidence of defective colour vision in the normal male population and in the series examined by Dr. Neubert. All I wished to do in this connection was to suggest an alternative explanation to that offered by the original author. This can hardly be classed as illogical.

The matter of fundamental importance is the interpretation of the data obtained from a completely unstandardised lantern. If one compares the results obtained with a single light lantern, and a lantern with three lights, the most obvious difference is the introduction of simultaneous contrast. If, in addition, one adds the variability of a rheostat control of illumination then without examining a single patient it is reasonable to suppose that the results obtained with the two types of lantern would differ. This is the conclusion one can reach while seated in an armchair by the fire and the results given by Dr. Neubert add nothing of value to this theoretical deduction so long as no attempt to standardise the lantern is made.

Yours sincerely,

JOHN GRIEVE.

MEDICAL SCHOOL, DUNDEE,  
November 10, 1947.

[Dr. F. R. Neubert does not consider a reply is necessary.]

This correspondence is now closed.—Editors.

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## POST-OPERATIVE SECURITY IN CATARACT CASES

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—With reference to Mr. A. J. Boase's letter in your December issue: I quite agree that a hyphaema may possibly form and be absorbed before the conjunctiva retracts and so escape notice. I have a feeling that the well-being of the patient should take a second place to statistics.

On the point that Mr. Boase raises regarding the possible failure to observe a hypopyon early, I can only say that I have had no infection in any of my cases as yet, but should it occur I would expect to observe the usual accompanying symptoms of pain, or discomfort, chemosis, etc. These would be definite indications for cutting the purse-string suture in order to examine the anterior chamber.

A further point with regard to the purse-string suture which appears to be worth mentioning is that, if silk or nylon is used the suture has to be cut—at whatever day the surgeon decides—whereas with the original catgut suture, nature will do her own work.

Yours faithfully,

T. G. WYNNE PARRY.

69, HIGH STREET,  
BANGOR, N. WALES  
December 15, 1947.

## NOTES

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Death                      AS we go to press we learn with deep regret of the death of Sir Henry Lindo Ferguson, C.M.G. of Dunedin, New Zealand. We hope to publish a memoir of him in a later number.

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Honour                      IN the New Year's Honours List we are pleased to see that Air Commodore P. C. Livingston receives the C.B.

\*       \*       \*       \*

The Ophthalmological Society of the United Kingdom. Annual Congress, 1948                      THE Annual Congress of the Ophthalmological Society will be held at the Royal Society of Medicine, 1 Wimpole Street, London, W.1, on April 8, 9 and 10, 1948.

The subject for discussion will be "Subjective Disorders of Vision (excluding those due to local ocular disease)," which will be opened by Dr. Macdonald Critchley, Professor Henry Cohen and Mr. J. H. Doggart. Members who desire to take part in the subsequent discussion are not required to intimate their intention before the Congress. It is emphasized that no member may speak for more than ten minutes.

On this occasion the Bowman Lecture will be delivered by Professor Marc Amsler, Zurich.

Members wishing to read papers are asked to send the titles to Mr. Lyle as soon as possible. Abstracts of papers, which will be circulated at the Congress and subsequently to the leading ophthalmological journals abroad, should be submitted not later than January 31, 1948.

On Friday afternoon there will be a joint Clinical Meeting with the Ophthalmological Section of the Royal Society of Medicine at the Ophthalmic Institute, Central London Ophthalmic Hospital, Judd Street, London, W.C.1. Those who wish to show cases are asked to communicate with the Registrar-Tutor, Mr. H. Ryan, at the Hospital.

The Annual Dinner will be held at the Royal College of Surgeons on Thursday, April 8. Owing to official restrictions the numbers on this occasion will be limited to 100, and it is regretted that it will not be possible to allow members to bring guests.

On account of the difficulty in obtaining hotel accommodation in

London, all members who will require it are advised to make their arrangements in good time.

*Honorary Secretaries* { E. F. King. (Council Business)  
T. Keith Lyle (Congress Business)

THE Society holds a considerable stock of certain volumes of the Transactions since their first publication. The following years, however, are not available :—

1897 ; 1898 ; 1899 ; 1900 ; 1901 ; 1902 ; 1905 ; 1906 ;  
1907 ; 1908 ; 1909 ; 1911 ; 1917 ; 1918 ; 1919 ; 1920 ;  
1921 ; 1922 ; 1923 ; 1924 ; 1926 ; 1927 ; 1928 ; 1929 ;  
1930 ; 1931 ; 1932 ; 1933 ; 1934 ; 1935 ; 1937 (Part I).

The Council feels that many libraries, both at home and abroad, may wish to complete their sets and will be glad to present to Libraries, Medical Schools and Hospitals such available volumes as they may desire. No charge will be made other than the cost of postage.

Those interested are asked to communicate with The Bowman Librarian, The Royal Society of Medicine, 1, Wimpole Street, London, W.1.

\* \* \* \*

*Sociedade de Oftalmologia de S. Paulo.* THE following are the officers for the year May, 1947 to May, 1948. *President* :—Dr. Benedito Paula Santos Filho ; *Vice-President* :—Dr. Plinio Toledo Piza ; *Secretary-General* :—Dr. Paulo Braga Magalhães ; *Secretary* :—Dr. Rubens Belfort Mattos ; *Editor* :—Dr. Alcides Del Ciello ; *Treasurer* :—Dr. Aureliano Fonseca.

\* \* \* \*

*Ophthalmological Society of Egypt* THE Annual Meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, on Friday and Saturday, March 12 and 13, 1948, at 9 a.m. Medical practitioners, oculists or otherwise, are cordially invited.

\* \* \* \*

*Oxford Ophthalmological Congress* THE next meeting of the Oxford Ophthalmological Congress will be held in Oxford, July 8 to 10, at the School of Geography, Mansfield Road. Accommodation for members has been arranged at Hertford College. The officers of the Congress are ; Master, F. A. Williamson-Noble ; Deputy Master, F. A. Anderson ; Editorial Secretary, L. P. Jameson Evans ; Hon. Secretary and Treasurer, I. C. Fraser, 12 St. John's Hill, Shrewsbury.

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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VOL. 32.

MARCH, 1948:

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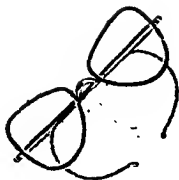
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LONDON:

THE BRITISH JOURNAL OF OPHTHALMOLOGY LTD.

24-27, THAYER STREET, W.1





TO HIS MAJESTY  
KING GEORGE VI



TO HER MAJESTY  
QUEEN MARY

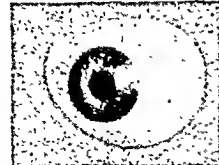
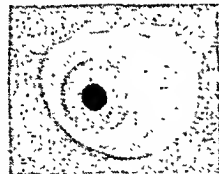
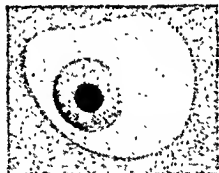
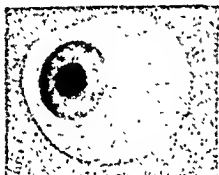
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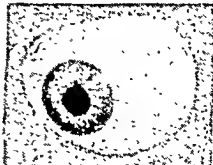
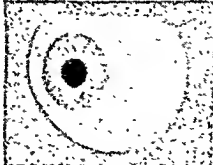
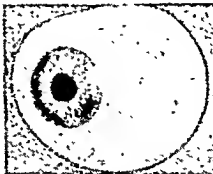
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## ARTIFICIAL EYES IN PLASTIC



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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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## A FURTHER CASE OF IRIDOSCHISIS\*

BY

ARNOLD LOEWENSTEIN

GLASGOW

JOHN FOSTER

LEEDS

and

S. K. SLEDGE

WAKEFIELD

IN a previous paper Loewenstein and Foster (*Brit. Jl. of Ophthal.*, 1945, Vol. XXX, p. 277) have described a rare case of a special kind of iris atrophy in which the ruptured radial fibres of the iris floated freely at one end in the aqueous. Consideration of the previously recorded cases (eight in number) in conjunction with our own led us to suggest *iridoschisis* as the best name for the condition.

Though we were fortunate enough to carry out the first histological investigation of the disease the cause remained obscure.

The case presented herewith exhibits similar though less marked changes and the description is supplemented by a coloured painting

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\* Received for publication, August 8, 1947.

by Mr. Gabriel Donald (Artist to the Tennent Institute, Glasgow), photographs of the clinical condition, and photomicrographs of a portion of iris removed at iridectomy.

### History

The patient, C.B., a railway shunter (aged 46 years), denied previous refractive error or eye trouble. The visual test imposed periodically by the railway company would tend to confirm this. When examined on January 30, 1947, as a workmen's compensation case (J.F.), he stated that exactly two years before he had fallen on the edge of a railway platform and broken his nose rather badly, the bridge being displaced to the left.

Apart from a "black eye" on the right side, he had noticed nothing wrong with his eye until ten weeks later when he accidentally noticed that the colour of the right iris seemed to have altered. Subsequently friends told him that "one of his eyes was hazel and the other blue." A certain diminution in the reading vision of the right eye occurring gradually since then led him to obtain reading glasses.

### On Examination

*Left eye.*—Vision = 6/12: with — 1.0 D.Cyl. 180° = 6/6.

The eye is normal. The iris is blue with a hazel colour at the pupillary border.

*Right eye.*—Vision = 6/12: with — 1.0 D.Cyl. 45° = 6/6.

The corneal endothelium is slightly opaque in the pupillary area.

The iris is a slightly darker blue with large areas of brownish atrophy most marked in the lower half, where the dark pigmented



FIG. 1.

Stereophoto of iridoschisis. Case No. 2.

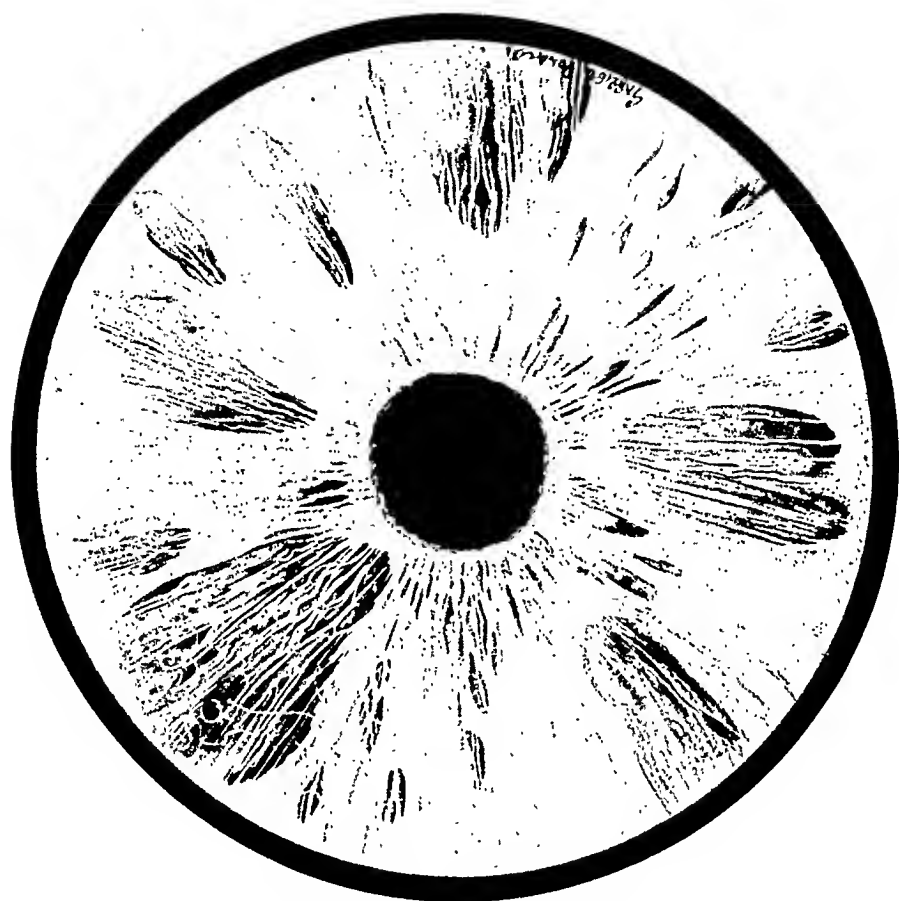


FIG. 2.



layers of the iris show clearly through the atrophic portion of the anterior layer. Here and there the fibres of the anterior layer of the iris have sprung away, and the pupillary ends of some of them have adhered to the posterior corneal surface near the limbus.

The pupil is oval, being larger below than above (Fig. 1).

The coloured plate (Fig. 2) gives a good idea of the slit-lamp appearance though omitting the adhesion of the fibres to the cornea. The lens, vitreous, and optic disc, were normal, though the tension was 35 mm. Hg Schiötz.

*Diagnosis.*—Iridoschisis and secondary glaucoma probably due to trauma.

*Treatment.*—May 23, 1947.

A basal iridectomy was performed on account of the high tension (S.K.S.), the excised iris being preserved in formol saline.

Recovery was uneventful and the corrected vision in this eye was 6/9 and J.1 at the time of writing, July, 1947.

*Biopsy.*—The obstinate tendency of the excised iris to curl in formol saline makes it difficult to establish the structural arrangements of the tissue exactly.



FIG. 3.

Curled up iris obtained by iridectomy. Note: sphincteric portion unchanged—shrunk thinned ciliary part cut twice—dilator well preserved—the entire anterior iris tissue is absent.

The pupillary portion of the iris is relatively intact, but contains more nuclei than usual. These nuclei are thickly covered with pigment, a common finding in dark irides, and frequently observed in naevi. (Fig. 3, photomicro).

There are dense collections of clump cells at the peripheral margin of the sphincter.

The papillary appearance of iris surface may be due to curling of the iris after excision.

The ciliary portion of the iris is much thinned, revealing hyaline degeneration of the iris tissue with well-preserved vessels; the pigmented dilator is intact everywhere.

The surface in contact with the aqueous shows a condensation of the tissue though not covered by endothelium.

Such gaps as are visible in this tissue suggest artefacts rather than natural openings to permit of aqueous absorption, as assumed by Carl Hamburger in his much-debated doctrine of ocular metabolism.

Naturally endothelial cells at the iris surface are less regularly arranged than corneal endothelium.

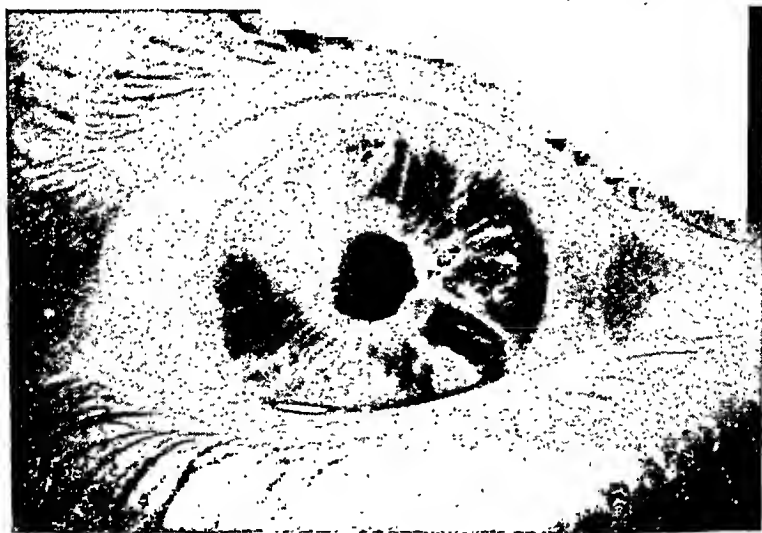


FIG. 4.

Similar fine granules can be found in the endothelial cells of the cornea as a sequel of phagocytic activity.

There was histological evidence in our previous case (*Brit. Jl. of Ophthal.*, 1945, Vol. XXX, p. 277) that the meshwork of Schlemm's canal was covered with pigment of a density even greater than one

would expect in a woman of 76 with cyclitic glaucoma. No gonioscopic or pathological examination of the angle made for pigment infiltration was performed in this, our second case.

### Discussion

While the excised portion of iris in our second case fails to show the gross horizontal split found in the first, the degeneration is further advanced in another respect, as bio-microscopy shows the spongy portion of the iris to be absorbed over a far greater area.

We regard this case as traumatic, and assume that the force which drove the aqueous into the spongy portion of iris was considerable, as in Schoenberg's case. Here the patient habitually dived into water from a height of a hundred feet.

One would expect the rate of degeneration to be slower, where the entry of aqueous was due to senile causes, as in the majority of the published cases.

The same mechanism may be in action in slighter degrees of iris atrophy, for example that seen in long-standing glaucoma.

Here the anterior layers shrink secondarily and draw the pupillary layer outward by cicatricial action, not infrequently producing ectropion uveae.

It is possible that the integrity of the iris stroma depends on the exclusion of the proteolytic enzymes of the aqueous by an intact surface layer. This is certainly the case in the cornea, where Holt and Cogan have demonstrated by electrical methods (*Arch. of Ophthalm.*, Vol. XXXV, p. 292, 1946), that the permeability of the structure depends on the state of the endothelium.

The progressive opacity and swelling of both lens and cornea in the presence of an unhealed breach of their surface membrane are, of course, well known.

One would expect such a lysis of the iris tissue to load the aqueous with pigment, with the possibility, as in long-standing cyclitis, of ultimate blockage of the drainage channels of the trabeculum.

On the other hand, changes of this type do not follow an ordinary iridectomy, where the access of aqueous to iris tissue may be quite extensive.

The probable explanation of this is that a rapid and marked retraction of iris vessels and fibres takes place at the site of the cut, and that the actual infiltration of aqueous is less than after the blunt injury described in which the iris split produced by the intruding aqueous follows the line of least resistance, *i.e.*, parallel to the iris surface.

That the retraction after iridectomy is marked can be judged by the rarity of iris haemorrhage after this operation.

It is an interesting fact that in our first case the floating iris



threads which had resisted proteolysis better than the spongy iris tissue, each contained a blood vessel whose lumen was filled with red blood corpuscles.

### Summary

A further case of iridoschisis is described. Pathological investigation of the iris has added nothing to our previous knowledge.

It is suggested that a blunt trauma forced the aqueous into the spongy iris tissue where the contained proteolytic enzymes destroyed the stroma. The pigment thus liberated blocked the drainage channels with production of secondary glaucoma.

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## A CROSS-SECTIONAL VIEW OF INJURIES IN AN OPHTHALMIC PRACTICE IN EIRE\*

BY

EUPHAN MAXWELL

DUBLIN

THE injuries recorded in this paper were serious in themselves or in their sequelae. In order to emphasise certain aspects of the subject as a whole, a few trivial injuries have been included, but apart from this, as the title serves to explain, there has been no selection of cases.

The records in the Royal Victoria Eye and Ear Hospital, Dublin, have been preserved since 1904, the year in which the Hospital commenced to function. It is from such of these as deal with the patients treated in that department with which I have been connected directly or indirectly, and during certain years chosen at random, that my data have been collected. The years in question were 1904-5; 1914-15; 1924-25; and 1939-45; all inclusive. I have also included case histories from my private records together with such as were still available from those of my father.

As many of the injuries antedated the case-histories by intervals of time varying from days to years, the period under review has been found to extend over three-quarters of a century.

### 1.—Causation

The injuries, 796 in number, have been arranged in this section in age-groups. Percentages noted here as elsewhere must be

\* Received for publication, October 20, 1947.

accepted as merely approximate. Causation introduces the subject of prevention but I have confined my attention in this respect to such problems as seemed to me, while analysing the cases, peculiarly relevant to the age-group under consideration.

*Birth injuries.*—Only 4 cases, all of them associated with forceps delivery, were recorded. Doubtless other conditions, examined during the period, due to birth trauma were missed, histories being seldom obtainable unless cases are seen shortly after the event. A discussion on preventive measures here would be outside the scope of the paper.

*Up to 4 years of age.*—Injuries amounted in this group to 4 per cent. of the whole, 66 per cent. being males and 34 per cent. females. Sharp objects especially with a glitter such as scissors, and falls in the vicinity of the domestic fire accounted for the majority. Organised preventive measures can hardly be expected to improve upon the maternal protective instinct but the "crèche" has justified its existence as an auxiliary in crowded areas where parents happen to find themselves in financial difficulties.

*4-6 years of age.*—Injuries amounted in this group to 5 per cent. of the whole, 65 per cent. being males and 35 per cent. females. Missiles such as sticks, stones, pieces of broken glass, etc., accounted for the majority. Children of this age delight in being allowed to join in the play of others older, stronger and I may add rougher than themselves—this often to their own hurt, to which the case histories bear ample testimony. To put too strong a curb on what is essentially a healthy instinct would be both unwise and difficult. Where supervision is unobtrusive the "playground centre" of the town and city has proved a valuable preventive measure in this direction.

*7-16 years of age.*—Injuries amounted in this group to 21 per cent. of the whole, 83 per cent. being males and 17 per cent. females. Games, organised and unorganised, many of the latter being more aptly termed hooliganism, accounted for nearly half the number.

A series of 27 cases (including some of the younger members of the next age-group) injured whilst playing games such as hockey, football, cricket, etc., has a local interest. Hurley as the national game can claim the largest proportion of casualties without prejudice, but 10 in the series seems unduly high. Moreover the aftermath makes grim reading—4 eyes had to be enucleated: 4 others suffered a total visual loss. The stick is the main danger, there being no rule, as in hockey, limiting the height to which it may be raised. If further evidence in this connection were forthcoming, the Gaelic Athletic Association

might consider it advisable to exercise stricter supervision over the small local games.

A series of 54 cases (including some of the older members of the preceding age-group) were injured in association with unorganised games. I use the word association advisedly as many of them were merely onlookers, with the end-result that they saw rather less than more of the game. Two small sub-groups deserve special mention. One consisted of twelve cases injured by air-gun pellets: three of the eyes had to be enucleated. I submit that, as in the case of fire-arms, air-guns should be licensed. The second consisted of eight cases injured by lime, mainly in the form of quick-lime mixed with sand, which had been thrown around in irresponsible fashion. It should be regarded as a criminal offence to leave dangerous materials unguarded in the public streets or builders' yards.

It is generally conceded that the closure of the so-called "dangerous gap" between the school-leaving age (14 in this country), and the entrance into industry would serve indirectly as a preventive measure in regard to injuries in this age-group:

• *17-45 years of age.*—Injuries amounted in this group to 46 per cent. of the whole, 90 per cent. being males and 10 per cent. females. Causes in this age-group reflect the industrial life of this country, where the main industry is agriculture. Metal splinters from farm implements, broken wire, nails, etc.—flying particles of stone in quarrying, road-making and repairing—thorns and branches in ditching and hedging accounted for the majority.

Nothing approaching the ideal protective device for the eyes for general purposes in industry has yet evolved, but the rapid development in "plastics" augurs well for the future.

Employers and employees will presumably agree in respect of certain essentials, viz., that the devices be comfortable and the material transparent, strong and not readily scratched or dimmed: that the shape be considered having regard to the occupation, the visor for example being the form of choice where danger is anticipated from above or from the side rather than from the front: that supplies should be plentiful and prices cheap.

It is unfortunate that few employers and employees recognise a joint responsibility in regard to maintenance: the one to renew stocks, the other to report defects. Several instances of faulty devices having not only failed to protect but actually having augmented injuries appeared in the case-histories. Such happenings naturally encourage the unreasoning prejudice against artificial protection which is still unfortunately very prevalent.

The recent establishment of a department of industrial ophthalmology in the Royal Eye Hospital, London, under the guidance

of Mr. Joseph Minton constitutes a major advance in these islands in regard to prevention in this age-group.

*46-65 years of age.*—Injuries amounted in this group to 20 per cent. of the whole, 83 per cent. being males and 17 per cent. females.

Similar causes to those in the last age-group accounted for the majority, though the relative incidence in regard to metal splinters was found to be much lower.

Presbyopia introduces a further problem in prevention. Hypermetropes should be encouraged to wear their "middle distance" correction while at work.

*Over 65 years of age.*—Injuries amounted in this group to 45 per cent. of the whole, 85 per cent. being males and 15 per cent. females. Misadventures whilst gathering and chopping sticks, and amongst the older people various stresses and strains accounted for the majority. Prevention here is largely a matter for the individual. He must accept the physical limitations imposed by advancing years and learn to adapt himself.

However neutrally inclined, no country escaped the repercussions of the second world war. Despite the small numbers involved, it was interesting to note how the result of analyses of the 526 cases recorded prior to 1940 and the 270 during 1940—45 fitted into the local picture which the general situation had rendered inevitable:—

An increase in the number of injuries associated with hooliganism.

A decline in the number of industrial injuries in the 17-45 age-group, with a corresponding increase amongst the older men and women together with boys between 14 and 16 years of age, as the result of emigration of young adults towards the war zone.

A sharp decline in the number of injuries associated with motor, and a rise in those associated with bicycle accidents, as a result of the shortage in petrol.

An increase in the number of injuries incurred whilst felling trees and cutting wood as a result of lack of domestic coal.

An increase in the number of injuries due to blunt or otherwise defective tools as a result of new stocks being unobtainable.

## 2.—Types of injury

Findings suitable for analysis in this section have been arranged in groups in order of their frequency.

(a) *Penetrating wounds of the globe*, omitting such as were caused by the entry of foreign bodies, accounted for 36 per cent., the majority being corneal or corneo-scleral. They were mainly

in the lower segment in accordance with the upward protective reflex of the eye: uveal involvement was noted in 55 per cent. and associated cataract in 50·5 per cent. of the cases. The few wounds of the sclera recorded were found in the main in association with wounds of the lids.

(b) *Contusions of the globe* accounted for 22·25 per cent., multiple effects in the same eye being frequently observed.

Under this heading affections of the *lens* accounted for 30·5 per cent., dislocations being slightly more numerous than opacities.

Affections of the *iris* accounted for 19·25 per cent.

Affections of the *retina* accounted for 18·25 per cent., vascular disturbances predominating. Amongst these latter were two cases seen years after the injury, one with a hole at the macula, the other with the anterior chamber full of cholesterolin crystals. A few instances of detachment, "immediate" and "remote" were also recorded.

Affections of the *cornea* accounted for 10·5 per cent., the majority being instances of superficial oedema with subsequent development of sepsis, together with a few instances of recurrent erosion. A group of four cases with interstitial oedema, three the result of explosions and one of an air-gun pellet deserves special mention. While rupture of Descemet's membrane was only confirmed on the slit-lamp in one instance, the cases would appear to have conformed with the clinical entity described by Major Dansey-Browning as "traumatic keratitis" in his papers on "battle casualties." (The Value of Ophthalmic Treatment in the Field. British Journal of Ophthalmology, 1944. Idem 1946.) In accordance with this author's experience the opacities took from two to three months to resolve.

*Ruptures of the sclera* accounted for 9·75 per cent. and of the *choroid* 8·25 per cent. One of the latter situated below the disc may be specially noted in that the retina was also ruptured resulting in an upper hemianopsia with sparing of fixation.

"*Contusions*" of the *optic nerve* accounted for 3·5 per cent., the term contusions being employed here in a wide sense to include defects secondary to trauma affecting the neighbourhood of the optic foramen.

(c) *Superficial wounds* accounted for 17 per cent., including a few instances where the lids alone were involved. As was to be expected the majority were corneal and were not seen until sepsis had developed. There were also a small number due to deeply imbedded foreign bodies, the most dramatic being a fish-hook which, blown backwards by the wind, buried itself, barb included,

in the cornea of a boy aged 15. Within three hours of the incident the hook was cut out, leaving a horizontal wound above the optical centre—two years later the vision with correction equalled 6/6 and J.1.

(d) Burns accounted for 8 per cent., of which 60 per cent. were due to lime compounds.

(e) *Foreign bodies which had passed into or through the globe* accounted for 5.75 per cent.

In 25 of the 42 cases recorded the foreign bodies had penetrated into the posterior part of the globe, the entrance wounds being in the main in the sclera. The lens was injured in at least 50 per cent. of the cases.

In 10 cases the foreign body came to rest in the anterior part of the globe.

The majority of the intra-ocular foreign bodies were magnetic.

In 7 cases the foreign bodies passed through the globe. These consisted of metal splinters, explosive materials and a rifle bullet. The routes were various. The globe was traversed in 4 instances in a fore and aft, in another in a lateral direction. The rifle bullet having penetrated the upper lid passed downwards through the globe ending half in and half out of the antrum of Highmore. Finally in the case of a man who had been stooping over a detonator which exploded, the foreign body entered the sclera below and, in emerging through it above wounded the inside of the upper lid, being then presumably washed away by the tears.

(f) Injuries involving the *orbit* accounted for 4.75 per cent. While the majority were haemorrhages or fractures, a small group of foreign bodies in the anterior part of the orbit, which caused little or no damage to the globe, have also been recorded. The fractures have been classified in accordance with the scheme outlined in the paper "Fractures of the orbit" by Major King and Lt.-Col. Samuel (*Trans. Ophthal. Soc. U.K., 1944*) with this result:—

*Lateral wall and floor*—8 cases, more than half being due to extensions from fractures of the maxilla and malar bones.

*Medial wall*—7 cases, 2 of which with an associated lacrimal fistula were the result of penetrating wounds.

*Roof*—5 cases, 3 of which were due to extensions from fracture of the base, one from fracture of the parietal bone, and the fifth from fracture of the upper orbital rim.

The diagnosis in these cases was based on clinical, and in so far as neighbouring bony structures were involved, radiological evidence. Unfortunately the average radiological reports on that

difficult region, the orbit itself, are seldom illuminating, and a further group of 8 cases with diplopia and in 3 instances proptosis, had to be accorded, in the absence of evidence to the contrary, a tentative diagnosis of haemorrhages in the orbit the result of contusion effects. To quote Lt.-Col. Samuel in the paper already referred to "the keystone of accurate diagnosis in these fractures lies in the use of a comprehensive radiological examination." As the majority of cases seen in an average civilian ophthalmic practice have sustained little structural damage, and treatment can be but conservative, it may be questioned, whether the expense of such an examination as a routine would be justifiable having regard to diagnosis only. On the other hand there can be no doubt that if prognosis is to be removed from the realm of speculation, knowledge of what has actually happened is essential.

(g) Injuries affecting the *cranium* with involvement of the visual apparatus accounted for 2 per cent., cases recorded in the series with merely post-traumatic neuroses not having been included. This low percentage would appear to be somewhat out of proportion but in Dublin, fortunate in its neuro-surgical unit under the leadership of Mr. Adams McConnell, such cases are referred for the most part to our colleague Mr. Alan Mooney, ophthalmic surgeon to the unit.

(h) Cases in which trauma, using the word in a broad sense, acted as a *precipitating* or *aggravating* agent accounted for 4.25 per cent. Unless the patient has been under previous observation the verdict where trauma is thus accused must be one of "non-proven." The doubtful standing of these cases in the survey has been acknowledged by placing the group last and out of the order of its frequency.

*Precipitation.*—Twelve instances of detachment of the retina in predisposed eyes and in which a history of preceding strain or comparatively trivial injury to the eye or its neighbourhood was obtained have been included under this heading. In 10 of these a medium or high myopia was present. The first of the two hypermetropes, a woman aged 56, having noticed a rapidly developing "blindness" of her right eye, recalled, after close questioning, that on the previous day she had received a knock on her right cheek. An examination of the eye revealed a detachment together with, in its neighbourhood but distinct from it, a peripheral area of retinal cystic degeneration. The second, a man aged 39, stated that his attention was directed to defective vision in his left eye by a blow on his head. Examination within a few days of the accident revealed an anterior dialysis in the

lower temporal quadrant, the detached retina showing a "moth-eaten" appearance.

A small group of cases which developed severe keratitis following trivial injury to the globe, and in which a diagnosis of syphilis or tuberculosis was subsequently established, was recorded.

Two further instances may be noted. In the first, a man aged 50, the right lens dislocated upwards under the conjunctiva, without any apparent cause—two years later, a slight blow on the left eye precipitated a similar catastrophe. The second, a girl aged 19, was frightened, if not actually struck, by a piece of plaster falling off the ceiling. Shortly afterwards she developed "hysterical" blindness. On admission to hospital three weeks later, there was no light perception. Five minutes after receiving 1 per cent. solution of zinc sulphate in both eyes, the vision became and remained normal.

*Aggravation.*—A group of 6 cases in which a more or less trivial injury to the globe resulted in an acute attack of glaucoma was recorded. In 3 of these the evidence was in favour of a prior chronic simple glaucoma; in the remainder a subsequent microscopical examination revealed the presence of intra-ocular tumour.

Two further examples were noted. The first was that of a young man who noticed visual defects in his right eye subsequent to a fall on the back of his head. The findings suggested an intra-cranial disturbance, confirmed later by an operation which revealed the presence of a hook-worm cyst in the left occipital lobe (this case was published in the Proceedings of the annual meeting of the British Medical Association in Dublin in 1933). The second was that of a boy who developed paralysis of the left 6th and 7th nerves following the blow of a cricket ball on his left cheek. Later his general condition began to show signs of deterioration and commencing bilateral papilloedema was observed. At the subsequent autopsy multiple intra-cranial tuberculomata were found.

### 3.—Observations on treatment and long-term histories

Prompt antiseptic treatment, general and local, is obviously the primary consideration in eye injuries. It is gratifying to note the gradual rise throughout the period under review of the efficacy of the antiseptics in use, a rise which mounted rapidly towards the close with the advent of the sulphur compounds and penicillin. Unfortunately there has been no marked reduction in the dangerous time-lag between the injury and initial medical treatment, in so far as all events as the rural community is concerned.



It must be admitted that difficulties of transport, accentuated during the second World War, have been a contributory factor, but the case histories have indicated time and again that the negative attitude of mind of the patient himself has been in the main responsible. Any attempt to combat this attitude must focus on two factors which tend to engender a false sense of security—lack in general of severe pain in wounds of the eye-ball unless and until sepsis supervene, and failure to appreciate the significance, or even become aware of defective vision in the injured eye in the presence of good vision in the sound one.

While the potential value of non-specific protein shock therapy had long been appreciated, it was not until about 1938 that, in the form of intravenous injections of T.A.B. vaccine, it began to be extensively used, and with increasing enthusiasm, by Dublin ophthalmologists. Its place, more especially in conditions tending to chronicity, is now assured. Obviously such a vigorous form of treatment is contraindicated in debilitated states, nor is it surprising that even in healthy persons it may produce considerable general, though temporary, discomfort. At the time of writing I have, however, only met with one instance of ocular complication, viz., herpes of the cornea followed by an obstinate dendritic ulcer in the uninjured eye of a boy aged 9.

The period has also witnessed that extraordinary advance in local and general anaesthesia which has rendered possible a precision in operative technique hitherto unobtainable.

On analysis the following cases and groups of cases emerged as suitable for comment in some detail:—

*Anterior synechia.*—From 144 cases of iris prolapse reported during the period a group of 30 in which no attempt at division of synechiae had been made, were observed over periods averaging 22 years. Twenty of these were noted to have suffered no discomfort though in two instances where the wounds had occurred at the limbus small implantation cysts had developed. In 16 cases where the synechiae were situated more or less peripherally vision was unaffected: in the other 4 where they were more or less central there was inevitably some reduction.

In the 10 remaining cases the vision was very reduced and some of the eyes had to be subsequently enucleated on account of painful scars or secondary glaucoma. Two children, both aged 3 at the time of the injury, developed buphthalmos, with marked rise of tension, after an interval of one and three years respectively.

In connection with rise of tension the following case seen in the early years of the period may be cited. A boy aged 9 developed a cataract as the result of a blow from a bush, no wound being

noted. A linear extraction resulted in good vision with correction. When seen 4 years later he had an enlarged and hazy cornea and a tension of 58 mm. Hg. No suggestions as to the cause of this development were recorded and there was unfortunately no "follow-up." While the wounds in this group were on the whole more extensive than in the former, it is of interest to note that it contained a higher proportion of young children.

Operation for the division of anterior synechiae may prove difficult; it can be still more difficult to decide whether an operation should be attempted at all. While the cases in which the synechiae were divided proved too few in number to permit of comparison, this "follow-up" may be said to favour conservatism. On the other hand it serves as far as it goes to emphasise the potential danger of gradual deformation of the globe in young eyes. It is unfortunate that in just such cases the whole problem is aggravated by the natural reluctance of parents to consent to operation on an eye which would appear to have survived the injury, for the sake of a problematic disaster in the future.

*Lental affections.*—In an analysis of 88 cases of cataract in which the eyes were either enucleated, or, where saved, kept under observation for periods averaging 7 years, 2 groups emerged of interest in connection with the time element in operative interference on the lens. In the first where no operation was performed, nearly half the eyes were subsequently enucleated. In the second where operation was performed within a few days of the injury the proportion of enucleations was still higher. In the absence of an analysis of all the factors involved it would be absurd to attempt more than a suggestion that at least some of these operations were of the nature of what is rather brutally described as "meddlesome" surgery. The results where every effort was made to combat rise of tension and iritic irritability by a vigorous use of therapeutics, and operation was deferred until a later date, were much more satisfactory.

Several instances of that disappointing though fortunately infrequent sequel, a tough thick capsule were noted, including cases of rethickening after division. To obtain an adequate opening may not only prove difficult, but be followed by undesirable reaction. Early and, where necessary, repeated division is the obvious course, but co-operation is not always forthcoming. For some time I have been considering the question whether an operation a few days after an X-Ray "contact" exposure, when the capsular tissue would probably be in a preliminary stage of softening, might present less difficulty. Recently with the kind co-operation of Dr. Sholto Douglas (Assist. Radiologist St.

Anne's City Hospital) I operated on a capsule, the toughness of which had already been demonstrated, a week after such an exposure, and with an encouraging result.

A series of 31 cases of *dislocation* were recorded but it is probable that minor instances of this condition passed undetected or were not entered in the case-sheets. Only 17 were examined in the initial stage, on an average, 14 days after the injury. In 3 of these cases the lens was successfully extracted, but in a fourth the attempt was followed by copious loss of vitreous and the eye became a total loss. One of the eyes which developed secondary glaucoma was trephined but while this operation succeeded in reducing tension the lens eventually fell back into the vitreous chamber, a general deterioration continued, and 5 years later phthisis bulbi was noted.

Eleven other cases in the series were examined at intervals, averaging 5 years after the injury. In this group 7 eyes were found at the final examination to have completely deteriorated. Two of the remaining 4, which can be said to have held their own, may be noted in some detail. The first was that of a man aged 41 who stated that 4 years previously his right eye had been injured by a stick. The findings consisted of a lens dislocated towards the nasal side, together with strands of suspensory ligament with zonular lamella attachments descending from behind the iris on the temporal side swaying to and fro in the anterior chamber. The vitreous face was unbroken. The vision with the pupil dilated and aphakic correction was normal. The second was that of a woman aged 55 whose right eye was struck by a piece of wood while chopping. An examination within a few hours of the incident revealed a lens dislocated towards the temporal side with vitreous in the anterior chamber. When examined 5 years later the lens, anchored by the inferior suspensory ligament, was seen to be lying in a horizontal backward position, presenting the appearance of an opened trap-door. Her vision, with aphakic correction, was still normal.

*Penetrating foreign bodies.*—An analysis of the 42 cases recorded showed that in the group of 7 in which the foreign body had passed through the globe 3 eyes had to be enucleated; 3, observed over an average period of 9 years, had very reduced vision but "quiet" eyes, while the seventh, in which the foreign body had passed out of the palpebral fissure (as noted in section 2), had practically normal vision when examined 5 years later.

In the group of 10 cases in which the foreign body had lodged in the anterior segment, it was extracted by the magnet or a forceps with satisfactory results in 8 cases. In 1 of the 2 failures the immediate result following extraction by the magnet was good

but a recurrent iritis associated with chronic colitis developed and the eye examined 27 years later was found to be blind and glaucomatous. The second failure was due to the patient's refusal to have the foreign body which had lodged in the anterior part of the lens, extracted. A few weeks later it had shifted to a position behind the iris whereupon the eye became painful. Magnet extraction failed to relieve the general condition of the eye and it had to be removed.

The record of the 25 cases in which the foreign body had lodged in the posterior segment is a sorry one, the ultimate condition in 16 eyes necessitating enucleation. In 6 of these 16 cases, the foreign body was non-magnetic and the state of the eye too dangerous to consider any attempt at extraction: in the remainder, although the foreign bodies were successfully extracted sepsis developed subsequently. It is interesting to note that in some of these cases, with the hope of minimising the danger of sepsis by reducing the time-lag, the magnet was used almost immediately on admission to hospital without awaiting an X-Ray examination. Modern therapeutics leave no excuse for such injudicious haste. All the magnetic extractions noted were by the anterior route. I have only recently adopted the posterior route and my practical experience is therefore limited. As far as it goes, however, it has strengthened my conviction previously based on theoretical considerations, that the posterior is the route of choice.

Two cases have an interest of their own. One, the only instance recorded in the series of extraction of a non-magnetic foreign body from the posterior segment, was that of a girl aged 14, whose left eye was struck by a piece of brass which came to rest in the vitreous in the neighbourhood of the pars plana of the ciliary body. It was removed by a cross action forceps through a scleral incision, and apart from incipient senile cataract, the eye when seen 47 years later, was normal with 6/9 and with correction J. 2. In the second, an example of disintegration of metal splinters, the initial X-Ray revealed an intra-orbital and intra-ocular foreign body. Two years after the injury siderosis was recorded and, 2 years later again, its disappearance. A slight attack of iritis in the eye 14 years after the injury brought the patient to the hospital and thus afforded an opportunity for a second X-Ray. This revealed complete disappearance of the intra-ocular and a definite reduction in the size of the intra-orbital foreign body.

*Retinal detachment.*—The number of "traumatic" cases noted under "contusion effects" (section 2) was 11, just under 1.5 per cent. of all the injuries recorded in the series. This percentage seems low but it must be admitted that my interpretation of what

constitutes traumatic detachment is somewhat rigid and open to criticism. Two of these cases may be specially noted, the first being that of a boy aged 15 whose left eye was struck by a stone. He was seen 6 years later with partial spontaneous reattachment of the retina. This case has been recorded in detail in the Transactions of the Ophthalmological Society, 1945. The second, despite a time-lag, afforded what would appear to be satisfactory evidence as to cause. A child, aged 8 years, in falling off a hayrick, struck her right eye on a binder. She was not seen until 4 months later when, in view of gross dislocation of the lens and bad light projection, it was decided to remove the eye. Microscopical examination revealed total retinal detachment together with definite traces of previous massive choroidal haemorrhages.

In view of the dramatic change in outlook which occurred during the period it is but fitting that some reference be made to surgical results. Unfortunately, for various reasons, the main one being that half of the patients were seen before the days of operation, only 4 cases from amongst those noted as due to, or precipitated by, trauma, had surgical treatment, obviously too small a number for any detailed comment. Suffice it to say that one of the eyes subsequently degenerated, possibly aggravated by too extensive scarring, while the other three, observed over periods ranging from 2 to 6 years, showed that a successful result had been maintained.

Not included in these groups were three instances of retinal detachment which had developed at the site of penetrating scleral wounds at intervals varying from 4 months to several years after the injury. No attempt at suturing these wounds had been made and these cases may be cited as evidence in favour of this procedure whenever possible.

*Sympathetic ophthalmia.*—Seven instances were recorded representing about 2 per cent. of the penetrating wounds and ruptures of the globe in the series. It must be acknowledged, however, that in only 2 cases was the clinical diagnosis confirmed by microscopical evidence.

The youngest patient was 9, the oldest 71, while the average age of the remainder equalled 34 years.

The average time of development after the injury was 7 weeks. To this time-group may be added 2 cases which did not develop the condition but in which microscopical evidence of incipient sympathetic ophthalmia in the enucleated eyes was found. In 1, a man aged 51, the eye was removed 3 weeks and in the other, a man aged 21, 3 months after the injury.

Three cases were recorded in which the condition was not observed until several days had elapsed after enucleation, 2 of

these presenting further points of interest. In 1 the wound was superficial, but an ulcer had developed which perforated, the final result being panophthalmitis subsequent to which the eye was removed. The other a boy aged 9, was struck in the left eye with a knife by his sister. The parents had to be threatened with the attentions of the N.S.P.C.C. before permission for enucleation could be obtained. Nine days after, k.p. and papilloedema were observed in the right eye. This boy, unfortunate in his family, was fortunate in the conclusion. Two months later the eye was normal with vision 6/6.

The final visual results in the sympathizing eyes were varied: only 2 instances of total blindness were recorded.

In regard to treatment, therapeutics varied with a tendency in favour of the arsenical compounds, especially as a preventive measure in the case of "dangerous" eyes. In 1 case a cataract was subsequently successfully extracted from the sympathizing eye by Dr. Anderson, of Belfast, who is publishing a detailed account in the Transactions of the Ophthalmological Society, 1947.

Two further cases relative to the subject may be noted. One a boy aged 13 developed circumcorneal injection and photophobia in the right, 2 months after an injury which had resulted in a scleral rupture near the limbus in the left eye. A tentative diagnosis of iritis, possibly sympathetic in character, in the right eye was made and as the wound in the left was found to have become markedly contracted, that eye was removed. Periodic attacks continued, however, for about another 2 months when they finally ceased, leaving a healthy eye with no trace of any previous iritis. That was in 1915. At a later date the slit-lamp would have enabled the obvious diagnosis of "sympathetic irritation" to have been arrived at sooner. The second case was that of a man aged 55 who developed a mild irido-cyclitis in the right some 14 months after a penetrating corneal injury had been caused by a twig in the left eye. As this latter was tending to phthisis bulbi it was removed though, in view of the patient's general condition affording ample cause for the irido-cyclitis, the possibility of sympathetic ophthalmia was not seriously considered. This clinical view-point was subsequently confirmed by the microscopical findings in the injured eye of a cellular infiltration of the choroid, confined entirely to the inner layers.

*Burns.*—Two case-histories with special points of interest are worth noting. The first, 1 of 2 instances of "eclipse blindness" recorded, revealed an almost incredible ignorance when it is realised that the eclipse in question occurred as recently as 1942. A school boy, aged 11 years, was permitted, if not actively encouraged, to watch the eclipse "through his fingers" for the

space of an hour, with the result that the vision in the right eye was permanently reduced to 6/24. The second provided an example of the destructive action of cresol. A man aged 40, developed recurrent ulceration of the left cornea following a splash of tar while engaged on road repairs. When seen at the hospital 6 weeks after the injury the entire corneal epithelium was found to be loose. Various treatments, including an effort to protect the cornea with a contact lens, proved unavailing, an intractable iritis developed, and eventually at the patient's own wish, the eye was removed.

An increase in a more general appreciation of the preventive possibilities of early grafting in the treatment of caustic burns was already apparent before the close of the period. The introduction of the use of "amnio-plastin" in this connection has proved a notable advance. At the time of writing my experience with this membrane while limited, has been most encouraging.

*Injuries secondary to orbital disturbances.*—An analysis of the 9 cases of optic nerve involvement recorded showed marked reduction of vision in 6 instances. In 5 where the ultimate result was blindness or merely appreciation of hand movements in the eye, the defect had been noted by the patient in the early stages: in the sixth where the vision equalled 6/36, when examined a year later, the defect had not been noted until 6 weeks had elapsed since the injury. The initial violence was in the region of the temple in 4 cases, and in the other 2 of the zygomatic arch and of the forehead respectively. Apart from severe destruction of the lateral wall involving the external rectus in 1 case, there were no associated neuro-muscular disturbances in this group. Three cases with field defects were recorded. The first, a man aged 28, in falling off a motor bicycle, struck the left side of his head against the ground. The following day a left 3rd nerve paralysis and an inferior hemianopsia were noted—central vision was not affected. Four months later the 3rd nerve had recovered, the field defect was unchanged.

The second, a boy aged 16, sustained a palpable fracture of the left upper orbital rim. An examination of the left eye in connection with diplopia in the direction of the fracture was made a year later when an inferior sector defect was discovered. Central vision was not affected. A year later again all that remained of the sector defect was a small relative scotoma to 1/1000; and this too had disappeared at a final examination some months afterwards.

The third, a woman aged 67, sustained a deep wound above and to the temporal side of the left eye-brow—an X-Ray of the skull was negative. She noticed defective vision in her left eye some

days later, but it was not until three months had elapsed that slight pallor of the disc was observed, when perimetry revealed with 3/330 a normal field except for a slight depression in the infero-nasal quadrant and with 3/1000 a sector defect in that area. A year later both isopters were involved in the defect. Although it did not extend to the fixation point there was some indeterminate disturbance of central vision. Movements of the globe were never affected.

A group of 12 cases in which *limitation of ocular movements* was recorded proved capable of analysis in respect of cause and subsequent history. In 4 instances a limitation, not restricted to any one muscle or group of muscles, would appear to have been the result of mechanical obstruction—in two, where movement was restored within a month, probably due to haemorrhage—in 2, where limitation was still present some years later, to cicatrized tissue. There were 4 instances of direct trauma to an individual muscle, in 2, where the superior oblique was involved, recovery took place within about six months—in 2, where the external rectus was involved, in about a year in 1 case, but in the other there was no recovery and the patient when seen 30 years later, was found to have developed marked over-action of the internal rectus.

There were 3 instances of paralysis of the 3rd nerve with loss of sensation along individual branches of the 5th, presumably the result of disturbances in the neighbourhood of the superior orbital fissure—there were unfortunately no references to the 4th nerve in the notes. In 1 of these cases complete recovery had taken place within two months—in the second, lateral movements were rapidly restored but the vertical not until 4 months had elapsed—in the third, lateral movements had recovered in about 5 months, but 4 years later there was still some limitation of the vertical. References as to the ultimate recovery of the 5th nerve branches were vague but return of sensation was obviously slow. The last case in this group has been included amongst orbital injuries as the X-Ray report was of a fracture of the right parietal bone extending into the orbital roof. The ocular findings, bilateral paralysis of the 6th nerve associated with mild papilloedema, were obviously, however, the result of posteriorly situated disturbances—7 weeks later all signs and symptoms had disappeared.

A case of emphysema in an amateur boxer, who had been struck in the right eye near the nose during a match was recorded. An X-Ray 3 weeks later, revealed the orbit clear of air but in the meantime the incident had decided the patient to adopt another hobby.

The period has witnessed the development of plastic surgery as a speciality and 10-day problems of treatment include not only



the "how" but the "who." No more potent argument in favour of retaining this work for the ocular area in the hands of the eye surgeon could be advanced than the published results of Major Stallard and Mr. Foster (Discussion on Plastic Repair of the Lids, *Trans. Ophthal. Soc. U.K.*, 1945). The position in Eire, whose people have not suffered the wounds of war, is different, however, from that which pertains in the rest of the British Isles. In a group of 40 cases in the series which included in addition to orbital injuries, isolated traumata of the lids, and contractions of the socket where due to penetrating wounds, only 6 required anything in the nature of what might be termed a major plastic operation. Even the inclusion of non-traumatic cases would not materially alter the fact that the demand is small, and, naturally where this is the case, individual experience must remain limited and hospital facilities somewhat inadequate. Mr. Foster has translated a passage from *De Medicina* thus: "If too much of the lid is lost nothing will restore it; if the loss is slight cure is possible." I confess my reaction to the problem is to operate on the case where "cure is possible," and leave "nothing" to the plastic surgeon.

*Intracranial injuries involving the visual apparatus.* It may be recalled here that the period has witnessed the development of yet another speciality, neuro-surgery. From the first, co-operation between the ophthalmologist and neuro-surgeon has been of the closest—a co-operation which has yielded rich dividends.

As already noted (Section 2) only a few cases have been recorded in the series. These included 3 instances of subdural haematoma, all of which were subsequently operated upon by Mr. Adams McConnell. The first that of a man aged 37, was hit on the back of his head by a plank. Some days later he developed severe headaches, and subsequently his sight began to fail. He was not examined, however, until 6 months had elapsed when he was found to have a mild bilateral papilloedema, no light perception in the right and a markedly reduced vision in the left eye. A subdural haematoma on the right side was evacuated, an exploratory puncture on the left proving negative—the operation was followed by complete cessation of headache. Five years later optic atrophy of the right eye, and in the left a tubular field with vision 6/12 and J.2, was recorded. The second case was that of a man aged 40, who, knocked off his bicycle, hit the left side of his head against a bush. Some weeks later he developed diplopia and a throbbing in his head. An examination 3 months after the injury revealed bilateral 6th nerve paresis and mild papilloedema: central and peripheral vision were normal. Some weeks after evacuation of bilateral haematomata all adverse signs and

symptoms had disappeared. The third case would appear to be an instance of "tentorial pressure cone." The patient aged 30, in lifting a heavy weight fell, striking the back of his head against the ground. About 3 weeks later he developed diplopia, loss of memory and lethargy. Examination of his right eye revealed a dilated pupil, which proved transitory, paralysis of the internal rectus and a haziness of the lower margin of the optic nerve. Vertical movements were absent in both eyes. Central and peripheral vision were normal. A clear subdural fluid evacuated on both sides was followed by a rapid improvement of his general condition. About 3 months later the right internal rectus was found to be normal, but it was not until nearly a year had elapsed since the operation, that the bilateral vertical movements were fully restored.

*Concomitant squint as a sequel.*—This development is not always recorded and only 24 cases in the series proved capable of analysis in regard to the association between position and the age of the patient when the eye was injured. The findings were found to conform more or less with those published in Worth's Squint—Chavasse.

Six eyes in persons under 3 years of age showed a divergence in 5, the 1 convergence being a late development.

Thirteen eyes in persons between 3 and 20 years of age showed a convergence in 8, 2 of which were aphakic with good corrected vision. Of the 5 divergent eyes, 2 were early and 3 late developments.

Five eyes in persons over twenty showed a convergence in one instance: of the four divergent eyes, two were early and two late developments.

#### 4.—Medico-legal aspects

The period witnessed the passing of the Workmen's Compensation Act, a measure of social reform of major importance.

In most of our cases the employer's liability is covered by an insurance company, which, in accordance with local usage, appoints an ophthalmic specialist to furnish a medical report. A workman can of course lodge an appeal against the compensation suggested, whereupon his case is heard in court. I submit that, while this court provides the best machinery for a discussion on the case as a whole, it fails in regard to the sifting of purely medical findings.

I suggest that if the medical report in the first instance were to be based as a routine upon a consultation between the doctor appointed by the insurance company and the doctor who treated the injury, there would be fewer appeals. I suggest further that,

in the event of an appeal, such a report might form a basis for a preliminary discussion over which an ophthalmic specialist appointed by the court as medical referee, would preside. If the judge, at the subsequent hearing, should desire further information, he would naturally request the doctors in question to attend as witnesses.

The working of the Act has tended to focus attention on a variety of problems connected with industrial injuries.

It may happen, for example, that to award a man who claims inability to resume his occupation, a lump sum of money, has the unhappy result of encouraging him to join the ranks of the permanent unemployables. When the difficulties associated with rehabilitation have been overcome it will assuredly be recognised eventually as the most humane method of compensation.

Its authors can hardly have anticipated the degree to which malingering may discredit the Act. Several instances were noted in the series, the following serving as an example. A man aged 44, who had lost his right eye some years previously as the result of an accident, developed a small ulcer in the lower part of the left cornea following a slight injury from a chip of paint. The ulcer healed without incident, and he returned to work, the vision in the eye with correction being normal. Two years later he reported inability to continue work as his sight had deteriorated and put forward a claim for £1,000. Despite the fact that he was able to walk alone to my house for an examination, he entered the study with the eye closed, feeling along the wall with both hands. Subsequently in court he forgot to play the part and moved about freely. Nevertheless his claim was settled "out of court" for £150: the easy way out. I submit that where the evidence in favour of malingering has sufficient weight, it should be incorporated in the medical report, when, at the discretion of the judge, the offender could be charged with attempting to obtain money under false pretences.

The major problems centre naturally around the protection of the workmen. Where negligence on the part of employers in respect of blunt tools, inadequate lighting and so on, can be demonstrated, the facts should be incorporated in the medical reports for the consideration of the court.

An important aspect of protection in the absence of the use of devices with side pieces, is a realisation of possible danger zones frequently complicated by the presence of a tyro or "accident-prone" workman. With this aspect in view I analysed a group of 215 cases, though in the frequent absence of valuable data the results could only be registered as impressions.

A workman's stance would appear to be determined by right

or left handedness, ocular dominance being of secondary importance. A right handed man engaged in work such as chopping wood, would tend to bring his right eye automatically into the main danger zone, in so far as foreign bodies flying more or less upwards were concerned: the analysis showed for this type of work a definite preponderance of injured right eyes. On the other hand if he is using a hammer and chisel, he tends to stand on the left side of his work, twisting the right side of his body downwards and forwards, bringing the left eye into the main danger zone: the analysis showed for this type of work a definite preponderance of injured left eyes. Foreign bodies may naturally fly off at various angles, rendering the matter of danger zones of equal importance to assistants and neighbouring workmen: a number of injuries thus incurred, appeared in the group. In this connection I was interested on the occasion of a visit to one of the small granite quarries in the Dublin mountains, to note the "safety" positions, relative to one another, adopted by the workmen. The owner informed me that these positions were firmly established in accordance with long tradition.

In the course of investigations in respect of the protection of the workman I have learnt to appreciate the importance of the foreman. A good foreman is the best possible interpreter of safety measures to his own group of men.

In conclusion I wish to acknowledge my indebtedness to Mr. William McCrea for his invaluable pathological reports. I would have asked him to supplement this paper with a comprehensive statement were he not already contemplating publication in respect of his work in the laboratory as a whole. I wish also to acknowledge my indebtedness to Mr. Harris Tomkin, who works with me in the same hospital department, for his permission to include in the series such of his patients as were admitted for treatment during the period under review.

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## A NOTE ON INTRA-VITREOUS PENICILLIN\*

BY

T. STUART-BLACK KELLY

MANCHESTER

SINCE clinical opportunities of administering penicillin by the intra-vitreous method are fortunately rare, these few cases may be of interest. The retinal changes described in experimental cases (Sorsby 1946, Mann 1946) and in some clinical cases (Rycroft 1945,

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Brown 1946, Mann 1946) make one hesitate to use the method at all, but most of these were treated before the articles mentioned appeared. A successful vitreous case following anterior chamber introduction (Cameron) and three similar successes (Nève, 1946) have been reported but are omitted from the discussion on account of their indirect introduction. At least twelve months have elapsed since the treatment was given and it was decided to try this method since it was felt that under the usual treatments (including penicillin in adrenalin sub-conjunctivally, Sorsby 1946), most of the eyes would have been lost.

The cases fall into four types, prophylactic, post traumatic vitreous infection, post operative vitreous infection and vitreous infection of unknown origin.

### Prophylactic

CASE 1. S. J. aged 48 years. Large magnetic intra-vitreous foreign body entered by scleral wound; highly probable chance of infection; removed by wound of entry; 1,000 units pure penicillin in 0.1 c.c. distilled water given via wound of entry into the vitreous; 50,000 units subconjunctivally with adrenalin, repeated once; usual intensive treatments; corr. V.A. on discharge 6/18; twelve months later, 6/9 J.I.

CASE 2. H.V. aged 5 years. Stone injury; wound in cornea, ciliary body and sclera (9mm.), iris incarcerated in c.b. and some prolapse of iris and vitreous; lens had disappeared; scleral sutures, excision of prolapses, conjunctival flap; 1,000 units given as in case 1.

This eye settled without any symptoms but because there was doubtful projection and the intra-ocular damage could not be assessed on account of intra-vitreous haemorrhage, and the effects of vitreous penicillin with regard to sympathetic ophthalmia were unknown, it was enucleated on the ninth day.

CASE 3. K.R. aged 28 years. Magnetic f.b. intra-vitreous ( $7 \times 6 \times 5$  mm.) via corneoscleral wound (6 mm.); iris and vitreous prolapse, lens not seen, removal by enlarged wound, corneal sutures, excision prolapse, and conjunctival flap. No vitreous was lost during the extraction of this large foreign body, probably indicating that the eye had already lost too much. Treatment was the same as in case 1, except that the vitreous penicillin was 2,000 units in 0.2 c.c. with 80,000 units subconjunctivally. Although the eye was symptomless and had good projection at times, it was enucleated because the projection varied and it was felt that the damage had been too great for useful vision. The eye was found to have only 1 c.c. of vitreous left, no lens, but no signs of infection or detachment.

## Post-traumatic infection

CASE 4. W.B. aged 14 years. Magnetic foreign body, intra-vitreous ( $4 \times 2 \times 1\frac{1}{2}$  mm.) via limbal wound 6 mm., early traumatic cataract. Magnet removal, no intra-vitreous penicillin; twenty-four hours later ocular pain, ciliary injection, hazy vitreous and poor projection suggested a vitreous infection. 2,000 units intra-vitreous penicillin given via wound as in case 1, with usual intensive treatment but no subconjunctival penicillin. In twenty-four hours symptoms had subsided, aqueous was macroscopically clear, projection fair. Five days later on sitting up a 'quiet' hypopyon appeared; lens continued to swell, but the eye still remained quiet with, however, only poor projection; enucleated on the fifteenth day, since it was felt that even if it stood a chance of recovery, the only fair projection combined with the unknown end result of intra-vitreous penicillin therapy might mean a liability to early sympathetic ophthalmia.

CASE 5. A.J. aged 33 years. Admitted with hypopyon, severe iritis and yellowish cloudy vitreous suggesting vitreous infection, apparently seven days old in a previously myopic eye of  $-18.0$  D.sph; found to have a magnetic intra-vitreous foreign body; removal via limbal section; treatment as in case 1, but with 10,000-units in 0.2 c.c. given in region of ora; symptoms subsided in twenty-four hours; tension low on discharge; twelve months later projection poor, secondary cataract, eye soft, but no signs of active disease. Refused enucleation.

CASE 6. M.S. aged 21 years. Admitted with hypopyon ulcer; found to have intra-vitreous magnetic foreign body ( $2 \times 1 \times 0.5$  mm.); vitreous haemorrhage, limbal wound, lens undamaged; magnet removal; usual intensive treatment (but without subconjunctival penicillin); hypopyon and symptoms began to subside; three days later a patch of exudate was seen behind the lens in the region of the wound, which gradually increased until five days later it had extended 5-6 mm. toward the posterior pole of the lens and the hypopyon had reappeared; 500 units penicillin given into the vitreous and 1,500 units subconjunctivally; hypopyon had gone by the next day, retro-lental exudate remained; 500 units repeated two weeks later on reappearance of hypopyon (the exudate had decreased only a little); discharged after six weeks with corr. V.A. 6/24. Readmitted two months later with 'quiet' hypopyon, no 'k.p.'; intensive treatment (but no subconjunctival penicillin); hypopyon went but reappeared seven days later; exudate still seen on lens; hypopyon cleared again only to reappear symptomlessly three months later; similar intensive treatment but with the addition of 50,000 units subconjunctival penicillin b.d. for two days. Evisceration advised because of probable chance of sympathetic ophthalmia. At

the evisceration the vitreous was removed intact with the anterior segment. The patch of exudate was found to be attached to a diffuse area of sterile pus in that region of the vitreous extending backward for about 6-8 mm. The rest of the vitreous was in good condition with an intact surface and no fluid.

CASE 7. S.R. aged 41 years. Admitted with five days history; yellowish vitreous haze; fibrous jelly like exudate in a.c. Marked iris exudate; bare P.L. Limbal removal of magnetic foreign body ( $5 \times 2 \times 1$  mm.); 1,000 units intra-vitreous penicillin in 0.2 c.c. given at the ora; P.L. improved to poor projection in five days; exudate in a.c. began to clear; enucleated on account of poor projection and possible subsequent danger on the fourteenth day.

### Post-operative infection

CASE 8. S. T. aged 70 years. Attempted intra-capsular extraction in which the capsule ruptured. Four days later severe iritis; intensive treatment begun including 50,000 subconjunctival penicillin with adrenalin; the next day a vitreous haze appeared, two days later the vitreous haze increased and became yellowish, projection became poor and a half size hypopyon had appeared: 1,500 intra-vitreous penicillin given via the ora and 90,000 units subconjunctival (adrenalin); symptoms and hypopyon had gone in 24 hours, vitreous still cloudy; discharged after three weeks with doubtful projection; three months later correction V.A. 6/60; twelve months later 2/60. He now shows a decrease in field corresponding to the injection area and the most dependent part of the vitreous; of which the apposite portions of the uvea show complete atrophy, and a single negligible floating vitreous opacity. The disc is atrophic to an extent suggestive of more damage than would be caused by arteriosclerosis (B.P. 200/100), when compared with the other eye, although this is not seen well on account of incipient cataract. Both have slight myopic changes ( $-5.0$  D. sph.). There is a central patch 5 mm. diameter in Descemet's membrane. It is probable that these degenerative changes are all the result of the infection and treatment.

### Panophthalmitis of unknown origin

CASE 9. S. C. aged 70 years. A controlled diabetic of some years, recently taken ill severely with no obvious cause; vitreous slowly became cloudy in one eye; followed exudate in pupil and dark cloudy aqueous; no treatment helped; only symptoms, lassitude and occasional pain; light perception eventually failed; evisceration attempted but choroid found firmly attached to a wrinkled sclera; enucleated. Following slow convalescence the remaining

eye affected similarly six months later; full medical investigations again negative; when perception had almost gone 500 units penicillin in 0.1 c.c. given via the ora; a.c. became clearer in 48 hours; vision returned to hand movements; no further improvement followed; death followed from an unknown cause three months later.

### Method of administration

A retrobulbar injection of 1 per cent. novocaine and 1/10,000 adrenalin is given into the anterior part of the muscle cone in all cases. In the traumatic cases 2,000 units pure penicillin in 0.2 c.c. distilled water are given into the affected region via the wound of entry or other suitable surgical opportunity.

In cases with no open wound a wait of five to ten minutes is essential to allow the capillary bed to contract. This will allow an intra-ocular space of approximately 0.1–0.3 c.c. Using a Record tuberculin syringe with a 20 bore needle a spot is selected about 8 mm. from the limbus at a point most appropriate for the lesion. The needle is twisted like a trephine until it sinks gently into the globe. Theoretically for future visual reasons it is better to allow the needle to sink only 5 mm. Should the cornea become slightly cloudy during injection the pressure is stopped and then the plunger is withdrawn slightly. This may not happen with 0.2 c.c. and no more should be given in any case. The needle is then withdrawn and the usual treatment resumed.

### Discussion

1. *Established infection.* The results of cases 6 and 8, the latter a man of seventy discharged with doubtful projection recovering to 6/60 in three months even including his subsequent central degeneration—and even cases 1, 3, 4 and 5 afford more hope than one would expect from previous results, owing perhaps to greater purity of the drug.

The almost inert physiology of the vitreous (Duke-Elder, 1932, Berens, 1936) serves as an incubator, but also allows a small amount of directly introduced antiseptic to be as effective as a large amount would be in any other tissue. It has been shown that no amount of systemic or local penicillin outside the vitreous will enter in sufficient strength to deal with more than a small infection which has been present more than 24 hours—(von Sallman, Meyer, di Grandi, 1944, Sorsby, Ungar, 1946), the most that can be expected is that the constant extra supply of infection exuding from the focus incubating in the vitreous will be kept in check as it reaches the uvea or aqueous—the vitreous meanwhile deteriorating chemically. Conversely, it would seem from these cases that to attack



the focus with a small enough dose to avoid general retinal and vitreous destruction; yet control the focus, may render the focus an inert mass which will be absorbed eventually like haemorrhage. Projection should theoretically be doubtful in cases which are really not so bad as they seem, since there will be a vitreous mass causing considerable light diffusion. Supporting this clinically, poor projection is sometimes seen in vitreous haemorrhage, and even in an a.c. exudate with a clear vitreous.

Isolated examples such as endophthalmitis have been cured by systemic treatment (Duke-Elder, 1947), some traumatic vitreous infections by protein shock, and one detachment with vitreous infection cured (6/6) by 150,000 units impure penicillin given orbitally in the operative region (Janus, 1945), but it is probable that the majority of cases of direct infection which have had no prophylaxis will be lost if no subconjunctival or vitreous treatment is given. Even subconjunctival therapy cannot be confidently used since the evidence probably appears after the incubation has reached a stage when only direct attack will suffice (Case 8).

Cases 1, 6, 8 suggest that on these principles retinal degeneration and optic atrophy might be avoided in otherwise normal eyes if treated early, useful vision remaining and justifying intra-vitreous penicillin in some infected vitreous conditions.

2. *Prophylaxis*. Is it justified however prophylactically? Many severely damaged eyes do recover without such treatment; cases, with large corneal wounds involving one or both ciliary regions and the vitreous, usually heal with an almost opaque cornea (partly due to sutures), and no lens. Since the life expectation of these individuals should see grafts commonly performed it is worth keeping these badly damaged non-irritant eyes even if they have only perception (sympathetic ophthalmia is discussed later). Infection occurred in this series of severe injuries in 20 per cent. probably corresponding to Desvignes and Boudon series. Since case 1 suggests that no deterioration will result (either due to the small quantity, purity, or dilution of the drug by the re-establishment of the circulation of the aqueous) and there is thus a chance of saving the infected 20 per cent., prophylactic treatment would seem justified.

Operatively the small vitreous volume even of 0.2 c.c. is less upsetting to a soft eye with a large corneal wound than a subconjunctival injection of 0.5 c.c. which occupies quite a large space and can deform the eye for a sufficient time to retard good immediate healing at the very time (first hour) it is most desirable. The normal physiology in any case is also greatly disturbed and the concentrations may not be as high as experimental evidence (Sorsby, Ungar, 1947) suggests. In small corneal wounds, of course, subconjunctival injections will be the best, and the concentrations will be in accordance with experimental evidence.

As a result, until further evidence is available a small prophylactic vitreous injection would seem justified in severe injuries.

Cases 5, 6 and 7, incidentally had impure penicillin.

3. *Vitreous Grafts.* Case 3 is of interest because in spite of hardly any vitreous remaining it settled with some projection. Had there been more vitreous it might have recovered. The only real objection to vitreous grafts in such cases would be infection. Perhaps it could be controlled by penicillin in protective solutions of small concentrations of, for example, 100 or 200 units per c.c.

4. *Uveitis.* It may be that the disappointing results in uveitis (Yasunā) are partly due to a certain amount of infection passing into the peripheral vitreous and acting as a constant focus. The rapid improvement shown by Weve's evacuation of "vitreous" exudate of localised patches of choroiditis by diathermy punctures (Weve, 1939) would suggest this. Intra-vitreous penicillin in generalised uveitis may perhaps be a future line of treatment rather than one to be avoided. Case 9, would appear to support this.

5. *Sympathetic Ophthalmia.* Perhaps it is unjustifiable to discuss sympathetic ophthalmia in relation to this small number of cases but since enucleation is mainly carried out with this in mind a few notes and queries are justified. First, in the prophylactic cases in which the penicillin may mask early sympathetic ophthalmia, is one justified in removal on purely varied projection? Will it be safe to wait until some irritant signs develop?

Similarly in the infected type the disconcerting suddenness of the cessation of symptoms and the continued quietude which follows, associated with the sepsis, presents a difficult prognostic problem. If the bases for the septic superstition were that either the local reaction was so severe that phthisis follows, or that the sepsis was sufficient to upset the infective or biochemical mechanism of sympathetic ophthalmia, then penicillin in these cases can be given no credit as a preventative. Does it follow that a septic case which has settled with penicillin is even better protected and can definitely be left until certain signs, preferably irritable, can be seen? Or should one assume that penicillin has stopped the septic prophylaxis before the process has been completed and the eye is therefore as prone to sympathetic as if sepsis had never been present?

In case 8, the waiting policy produced useful vision and it does not seem unreasonable to leave any case which was treated as soon as the vitreous infection was diagnosed to continue its course until definite irritative signs develop—none of which appeared in these cases although treatment was instituted later than it would be in a future case.

In all cases the advantage of the retrobulbar injection must be given credit. The near ischaemia during surgery is as useful as an

orthopaedic tourniquet, and the subsequent return of full circulation as a slow decompression is also useful, while the anaesthesia is incomparably better than a general.

### Conclusions

This series is of course far too small for any conclusions but the somewhat better results than most previous cases have shown, suggest a more hopeful future than has been expected. The following suggested treatments with pure penicillin are therefore purely a working basis for use until further evidence is available.

1. *Prophylactic.* In any trauma with a large corneal wound in which there is a probability of vitreous infection as judged from the circumstances of the injury.

2. *Post-traumatic and post-operative vitreous infection.* In any post-traumatic and post-operative vitreous infection that does not subside immediately with subconjunctival penicillin (adrenalin).

3. *Vitreous infection of unknown origin and generalised uveitis.* In any progressive vitreal condition which suggests an infection even of low grade, that is not amenable to subconjunctival (adrenalin) penicillin.

4. *Vitreous graft.* The possibilities of vitreous grafting controlled by penicillin might be considered.

5. *Dose.* 1,000–2,000 units of pure penicillin in 0.1–0.2 c.c. distilled water.

I wish to thank the Honorary Staff of the Manchester Royal Eye Hospital for permission to publish these cases.

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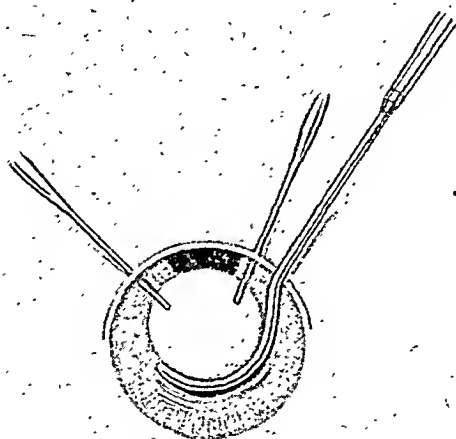
A COMPLICATION OF INTRACAPSULAR  
CATARACT EXTRACTION\*

BY

F. A. WILLIAMSON-NOBLE

LONDON

It occasionally happens during this operation, especially in relatively young patients in whom the zonule is tough, that the capsule ruptures. In these circumstances a portion of anterior capsule is removed in the forceps, leaving the rest of the lens behind. Attempts to express the lens, as in the extra-capsular operation, may be unsuccessful owing to the softness of the eyeball, which has been deliberately produced by pre-operative, retro-ocular injection. This



condition is of inestimable value in intracapsular extractions, because it obviates the danger of escape of vitreous, but it may prove a serious obstacle to expression of the lens, when some of the anterior capsule has been removed. What usually happens is that the lens can be expressed as far as the lips of the wound, but cannot be made to leave the eye. Careful manipulation with a vectis will sometimes effect this, but the use of this instrument increases the risk of intra-ocular infection and of vitreous loss.

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\* Received for publication, January 11, 1948.

It occurred to the writer once, when faced with this dilemma, to pass two cystitomes into the lens, broadside on, if necessary, steadying the latter during the procedure by gentle pressure with a squint hook held by an assistant (vide figure). The cataract, which was not a soft one, was then easily lifted out of the eye, and no complications ensued. This manoeuvre has been repeated in two other cases with successful results, and is simpler and probably safer than the use of the vectis.

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## AN ATTEMPT TO TREAT A PERFORATED EYE WITH SUBCONJUNCTIVAL PENICILLIN\*

BY

FRANK R. NEUBERT

GUERNSEY

*History.* September 17, 1947. Perforation of cornea by piece of wire which patient was cutting.

*Examination.* The eye was seen about three hours after injury. The cornea had a 3 mm. perforation at 1 o'clock halfway between the pole and limbus. Most of the aqueous was lost. There was no iris prolapse. A thin film of whitish exudate covered the pupil and the lens could not be seen although injury of it was considered likely.

September 18, 1947. There was a sticky conjunctival discharge. The aqueous appeared slightly cloudy. No pain.

September 19, 1947. The right eye was injected. Smear and culture of L.E. shows a small growth of Gram-positive penicillin-sensitive cocci. An attempt was made to save the eye by means of penicillin following the method of Sorsby and Ungar. ("Distribution of penicillin in the eye after subconjunctival injection" by Arnold Sorsby and J. Ungar, *Brit. Jl. of Ophthal.*, September, 1947). Mydracain was injected followed by penicillin 50,000 units in adrenalin and novutox subconjunctivally. A course of intra-muscular penicillin injections 30,000 units was commenced.

September 20, 1947. The corneal endothelium was almost opaque. The conjunctiva was very injected and the discharge still present. Subconjunctival injection of penicillin was repeated twice.

September 21, 1947. The conjunctival injection was increased and the cornea was quite dull. In view of the apparent deterioration the subconjunctival injections were discontinued. The intra-muscular injections were continued.

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\* Received for publication, December 12, 1947.

September 22, 1947. Two k.p. seen through the dense corneal haze. The eye was removed.

The socket was clean and healing was rapid; the man was discharged on the fifth day.

### Pathological Report

*Résumé.* Corneal epithelium shed. Anterior chamber contains k.p. and fibrinous exudate. Iris, oedematous and infiltrated. Lens cataractous: capsule ruptured and early abscess formation. Abscesses present in vitreous. Retina detached and undergoing necrosis.

*Diagnosis.* Early panophthalmitis.

*Remarks.* A case is reported of an injured eye infected with penicillin-sensitive organisms which did not respond to penicillin therapy.

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## THE USE OF ANTI-ALLERGIC DRUGS IN THE TREATMENT OF PHLYCTENULAR OPHTHALMIA \*

BY

C. F. BOWES

LONDON

THE striking success achieved by benadryl and allied drugs in the treatment of urticaria and a widely divided group of conditions of allergic origin, suggested that this group of drugs might give some alleviation of the photophobia, irritation, lacrimation and eczematous condition with which phlyctenular disease is associated.

### Subjects

Fifteen children from 2½ to 11 years of age. All had clinical evidence of phlyctenular disease, and showed positive Mantoux tests, and X-ray evidence of tuberculous infection; 9 cases had a family history of tuberculosis and 8 were contacts). In all cases the drug concerned was given when the symptoms were particularly troublesome and hence any improvement would have been particularly noticeable.

### Drugs used

The two drugs used were benadryl (Parke Davis and Co. Ltd.), and antistin (Ciba). In 7 cases both agents were employed after an interval of at least one week.

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\* Received for publication, November 25, 1947.

### Benadryl

This was used in 12 cases, a test dose of elixir benadryl (10 mgs. 1 drachm) was given 3 times a day the first day and then increased up to the amounts below:

	1 mg./lb.	2 mg./lb.	4 mg./lb.	body weight
No. of cases	2	4	6	

In all cases the total daily dosage was divided into three equal portions.

In only one case was there any improvement at all (4 mg./lb.) and as atropine was continued in all cases, the very slight amelioration of symptoms could easily have been due to the atropine.

No side effects were observed even at 4 mg./lb. body weight and the impression received, was that children were more immune to the symptoms of drowsiness, lassitude, etc., than were adults.

### Antistin

This was used in 10 cases and the dosage employed was 1 tablet 3 times a day for 6 cases. In 4 cases this was increased to 2 tablets 3 times a day.

There was no improvement in any of these cases and as opposed to benadryl the side effects, particularly of giddiness, were very noticeable.

### Conclusion

In 15 typical and active cases of phlyctenular ophthalmia, there was no improvement of the photophobia, lacrimation, irritation and eczema with benadryl and antistin, two well recognized anti-allergic drugs.

I am indebted to Professor Arnold Sorsby for permission to publish this note.

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## INTRA-MURAL NEW VESSELS IN AN OCCLUDED RETINAL VEIN

### A clinical description\*

BY

I. C. MICHAELSON

GLASGOW

THE following case is described because it illustrates clinically the presence of fine vessels within the wall of a retinal vein. So far as concerns the retina such intra-mural vessels have been described

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\* Received for publication, August 9, 1947.

histologically by Loewenstein (1946) and the ophthalmoscopic findings in this case appear to be complementary to his anatomical observations.

The female patient, aged 60 years, developed an obstruction of a branch of the superior temporal vein of the left eye close to the optic disc on November 11, 1946. The condition of the fundus on April 16, 1947 is illustrated in the figure. It shows the development of numerous collateral vessels between the affected and unaffected branches of the superior temporal vein. The more unusual development, however, can be seen in the ascending portion

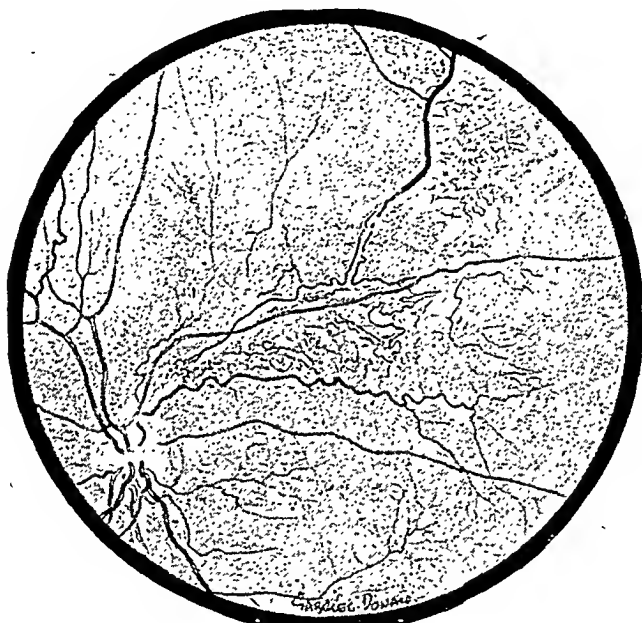


FIG. 1.

Case of thrombosis of a branch of the superior temporal vein showing the development of intra-mural new-formed blood vessels one of which is passing into a dilated capillary plexus which is draining into an unobstructed vein.

of the obstructed branch. On either side of the blood column a pale white sheathing can be seen, representing an opacification of the vessel wall. Where the blood column is attenuated and interrupted for a short distance there are two very fine vessels running close to the blood column in a parallel direction. These vessels are within the visible wall of the vein, one on each side of the lumen. The situation of these vessels can be defined even more clearly with the light from a mercury lamp. The vessel in the temporal part of the vessel wall can be seen leaving the vein after an intra-mural



course of about 1.5 mm. to pass into a dilated capillary plexus which is draining into the unobstructed vein. This intra-mural vessel is evidently facilitating drainage from the narrowed portion of the obstructed vein. Loewenstein in his histological studies notes that intra-mural vessels may run in the direction of the parent vessel and that they may leave it to pass into the general capillary system.

### Summary and Conclusions

(1). A clinical description is given of intra-mural new formed vessels in an obstructed vein.

(2). One of the purposes of such vessels is drainage from obstructed circulation into capillary plexuses situated favourably for the establishment of collateral circulation.

I am indebted to Mr. Gabriel Donald for his care with the illustration.

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## AN IMPLANT WITH BRIDGES FOR ATTACHMENT OF MUSCLES\*

BY

EMANUEL ROSEN

NEWARK, N.J.

THE new developments in plastic prostheses have so well solved the problems of colour and form matching as to emphasize the lack of movement which remains the chief defect in the present solution of this age-old problem. Movement of the prostheses in use or suggested is dependent upon the movement of the stump. The purpose of this article is to suggest a new surgical approach which utilizes the physiological and anatomical characteristics of the normal eye as far as possible.

The use of plastic substances particularly the methacrylic resins is not exactly a new venture in socket implantation for it has been considered by several authorities.<sup>1</sup> The substance is cheap, readily accessible and extremely adaptable. It is well tolerated within the orbit and can be prepared to conform with any desired shape. It can be finished smoothly or roughly as desired, both finishes being considered of benefit by certain sources. We are

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\*Received for publication, May 5, 1947.

cognizant of the great many materials which have been considered and used in artificial implantation and also how these materials have been discarded one by one. Our aim is to introduce a new surgical approach to implantation.

Since we propose herein only to introduce a new type of implant we shall not go into the evolution of our model with its many discarded suggestions but shall simply submit and describe our present model in the form of a preliminary report. The implant consists of a plastic truncated cone with a convex base. Its exact size is variable, the antero-posterior diameter being 18 to 24 mm. and the diameter of the convex base being 16 to 18 mm. Six bridges, which have been so situated on the basis of anatomical study, have been built upon the anterior convex surface around each of which the recti and oblique muscles are tied and sutured back upon themselves. Upon severing the tendons of all the extra-ocular muscles, double armed 0000 catgut sutures are placed in each muscle and put aside with a clamp. After enucleation and complete stoppage of hæmorrhage, the implant is placed in the socket and each muscle is drawn under its corresponding bridge to be sutured back upon itself and around the bridge thus producing a tunnel of muscle tissue. A definite attempt at muscle balance is made. When all recti muscles have been sutured back upon themselves Tenon's capsule comes back into proper anatomical position. The conjunctiva is then carefully sutured in a horizontal line with very close approximation of interrupted sutures. We realize that leaving Tenon's capsule open is a radical departure from any enucleation with implantation but muscle suturing to the bridges of the stump will retain the implant much better than overlaying the implant by suturing Tenon's capsule. The implant cannot be expelled and its mobility is unquestioned. We have endeavoured so to attach the muscle tendons that Tenon's capsule will resume its original anatomical position and the same feature is aimed at when suturing the conjunctiva.

The purpose of our implant is to secure the best possible movement attainable in restoration of a movable stump. Such a movable stump can be mechanically adapted for accurate fixation of a plastic prosthesis which feature has already been completely and adequately achieved. Side issues upon our implantation include the use of the alginate stencils in the socket so as to direct the method of reformation of the cul-de-sac and produce hæmostasis thus preventing the frequent complication of chemosis; and a course in orthoptics to keep the muscle tonus adequate. We are at present also considering and experimenting with various methods of fixation of the stump to the inner surface

of the prosthetic whereby the anterior end of the stump can be built up so that no element of exophthalmos will exist. In a later model we have replaced the plastic bridges with metallic bridges not so much to secure added strength as to have a method

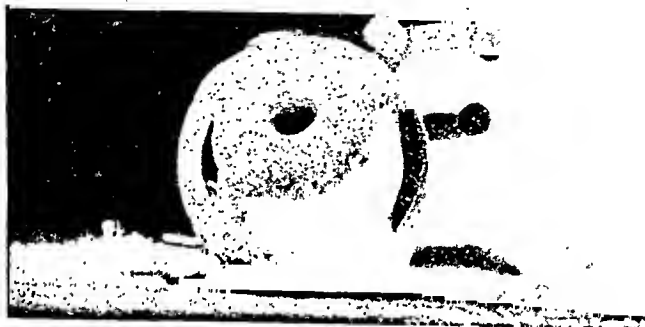


FIG. 1.



FIG. 2.

Figs. 1 and 2 show lateral and frontal view of the plastic implant with its bridges. The frontal view shows some perforations upon the surface of the implant.

of X-ray localization to observe any orbital shift of the implant. Having made a careful analysis of many sockets reformed by many of our leading ophthalmologists we wish to introduce this procedure as worth while and simple, realizing the great improvement of movement even at so early a date.

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CASE 1.—J.G., aged 26 years, had a complicated cataract of eight years duration secondary to an old iritis. The intra-ocular pressure measured 60 (Schiötz). He complained of headaches in the region of the right eye, pain in the eyeball and redness of his eye. Light projection was faulty. His was the first case in which the bridged implant was employed following enucleation, the operation being performed in November, 1944. In this first model no provision had been made for the oblique muscles and the tendons of the four recti only were attached to their respective posts. At the end of five days the eye was dressed at which time no chemosis whatsoever was observed of the conjunctival tissues. At the end of two weeks the conjunctiva had completely healed. There was no oedema or secretion. Motion, up, down, left and right were highly satisfactory. There was no suggestion of retraction of the conjunctiva upon the temporal side when looking nasally and vice versa. After two months the conjunctiva appeared quite normal and the movement could be considered very good.

CASE 2.—This patient, M., aged 24 years, sustained a penetrating injury to his right eyeball three years ago.<sup>2</sup> There was a "through and through" penetration of the eyeball. During enucleation a specific complication was observed in the external rectus muscle which had become quite fibrous and inelastic. This loss of elasticity led to a good deal of difficulty in securing the attachment of the external rectus to its respective bridge. Here again only the four recti muscles were attached to the bridges before closing the conjunctiva. Although much more oedema was present in the conjunctiva than was seen in the first case, this subsided almost completely at the end of two weeks. At the end of five weeks the conjunctiva was quite normal in appearance and the movement could be considered quite good except in the lateral direction. The implant seemed to lodge slightly upward and nasally but was not actually displaced. Movement parallels the remaining eye in all directions except in looking to the right temporal field.

CASE 3.—A.D., aged 22 years, had a shrunken globe resulting from a perforating glass injury some twelve years earlier. There were multiple staphylomata and X-ray indication of choroidal calcification. The cataractous lens was visible within a rather deep anterior chamber. Enucleation was technically difficult because of the rapid collapse of the globe in which hypotension had existed preoperatively. At any event, only the four recti muscles could be adequately secured to the bridged implant. The oblique attachments were unused. Oedema and chemosis were minimal and upon the ninth day the results were considered very

good from the standpoint of movement and from the general appearance of the conjunctival sac. At the end of two weeks the conjunctiva was completely healed with the "collar button" stud projecting through this structure and moving to all extremes of up, down, medial and lateral movement.

CASE 4.—J.T., aged 26 years, lost the sight of his left eye following a penetrating knife injury in childhood. The eye rapidly became shrunk, with deformed irregular cornea and multiple scleral staphylomata. X-ray report disclosed a calcification of the choroid of rather symmetrical appearance. There was ptosis of the left upper lid and retraction of the globe. The eye was enucleated in the usual manner. All six extra-ocular muscles were attached to their respective bridges and the conjunctiva was sutured about the "collar button stud" with two sutures running through the neck of the collar button stud to keep the conjunctiva snugly secured and thus prevent its riding upward. A negacoll mould was placed in the socket and retained for five days. At this time very little oedema was present and the implant appeared to be in good position. At the end of ten days the oedema had subsided; the conjunctiva was well united and the movement was excellent.

CASE 5.—J.S., aged 24 years, suffered a penetrating "through and through" corneal wound following an explosion of a bottle when he was fourteen years old. There had been recurrent attacks of pain and redness in his left eye for the past two years. The intra-ocular pressure was 42 (Schiötz). The iris was completely incarcerated in the vertical corneal wound being so drawn that no pupil and no anterior chamber was visible. The eye was enucleated and the extra-ocular muscles were attached to their respective bridges with the "collar button stud" being handled as in Case 4. Both Case 4 and Case 5 were operated upon the same day and results appear to be running parallel. At the end of two weeks the conjunctiva whitened; there was no oedema; the collar button stud was in good position and movement appeared to be unusually good.

Observation of our five cases over a six months period has tended to confirm our expectations. While only time can finally resolve the ultimate value of any new approach we feel that the well established physiological basis for what at first glance may appear to be radical, justifies our venture.

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# PATHOLOGY OF MUCOUS AND SALIVARY GLAND TUMOURS IN THE LACRIMAL GLAND AND THE RELATION TO EXTRA-ORBITAL MUCOUS AND SALIVARY GLAND TUMOURS\*†

(Studies on Orbital Tumours—3)

BY

ERIK GODTFREDSSEN

COPENHAGEN

## Introduction

MIXED tumours of the mucous and salivary gland types having recently been submitted to thorough revising investigations in Scandinavian literature (Therkelsen, 1934, Ahlbom, 1935, and Ringertz, 1938), the experiences from these investigations will be compared here with those gained from a series of cases of mixed tumours in the lacrimal gland. No studies of this kind are available, and histopathological parallelism does not *a priori* mean biological parallelism.

## Previous investigations into lacrimal gland tumours

The lacrimal gland tumours constitute about one-fourth of the comparatively rare orbital tumours (Birch-Hirschfeld 30 per cent., Sattler 25 per cent., and Godtfredsen 20 per cent.). The experience gained by the individual observer is, therefore, limited. The literature is chiefly casuistic or compilatory. Thus Warthin collected 132 cases (the literature up to 1901) and Lane 112 cases (the literature up to 1922). Scandinavian communications are scarce (Ehlers and Okkels, 1931).

The value of these papers is reduced by the heterogeneity of the different writers' histopathological estimations based on different views, particularly concerning the histogenetic conditions (ectodermal, mesodermal, or "mixed" genesis). The same heterogeneity prevails in the text-book literature (Meisner and Birch-Hirschfeld in Schieck and Brückner's text-book, Seidel and Peters in Hencke and Lubarsch's text-book).

The histogenetic conditions will not be discussed in detail, only it should just be mentioned that, according to the modern, revised view the genesis of mixed tumours is now regarded as purely

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† Received for publication, October 27, 1947.



ectodermal (or epithelial), (Ahlbom, Ewing, Kreyberg, Ringertz, Therkelsen). The apparently "mesenchymal" elements of the mixed tumours (fibrils, hyaline cartilage formation, etc.) are not mesodermal but ectodermal products of the epithelial cells which to a great extent undergo metaplasia, a.o. to squamous epithelium. The tumour-proliferating epithelium may, moreover, present all transitional forms from benign to malignant. These facts explain the great variations in the nomenclature (chondro-myxosarcoma, angio-reticulo-fibro-epithelioma, endothelioma, adenoid carcinoma, etc.). The term mixed tumour, now current in the literature and also used here, is thus actually inadequate, meaning strictly a tumour developed from different germ layers.

A clinically and histopathologically homogeneous impression from the literature is, therefore, out of the question. The frequency of malignant cases is difficult to estimate. Lane's report gives an approximative impression: Of 95 cases 12 died of the disease. There was recurrence in 20 per cent. and metastases occurred in 7 cases.

### **Main features of biology of extra-orbital mucous and salivary gland tumours**

A number of biological main features, of importance for the present study, from the recent Scandinavian investigations into mucous and salivary gland tumours will be briefly summed up.

The mucous and salivary gland tumours belong to the comparatively rare forms. They occur most often in the large salivary glands (parotid and submaxillary), where most of both Ahlbom's 254 cases and Therkelsen's 74 cases were localized. Each of these two series—collected over 24 and 20 years respectively—contained only one case of tumour in the lacrimal gland. Mucous and salivary gland tumours, developed from the glandular elements of the mucous membranes in the nose and paranasal sinuses, constituted 10 per cent. of Ringertz's 352 malignant cases. Localisation in the nasopharynx is rarer, constituting only about 1 per cent. of the malignant tumours here (5 of Godtfredsen's 432 verified cases, 1944). Confusion with parotid tumours is possible in these cases (Godtfredsen, 1947).

Mucous and salivary gland tumours may occur at any age, and there is no significant difference in sex. The past histories extend on an average over 2 years.

The histopathological main feature is the arrangement of the epithelium in alveolar groups, cords, or islands with an often considerable production of mucus extending partly into a central lumen in the alveolus and partly intracellularly and centrifugally,

thus causing bursting of the cell groups—and myxomatous degeneration. In addition to mucus the epithelial cells produce fibrils and hyaline substance, and different stages of hyaline cartilage formation may occur.

There are two histopathological main types: the fibro-myxo-epithelioma and the basalioma, which may both be either benign

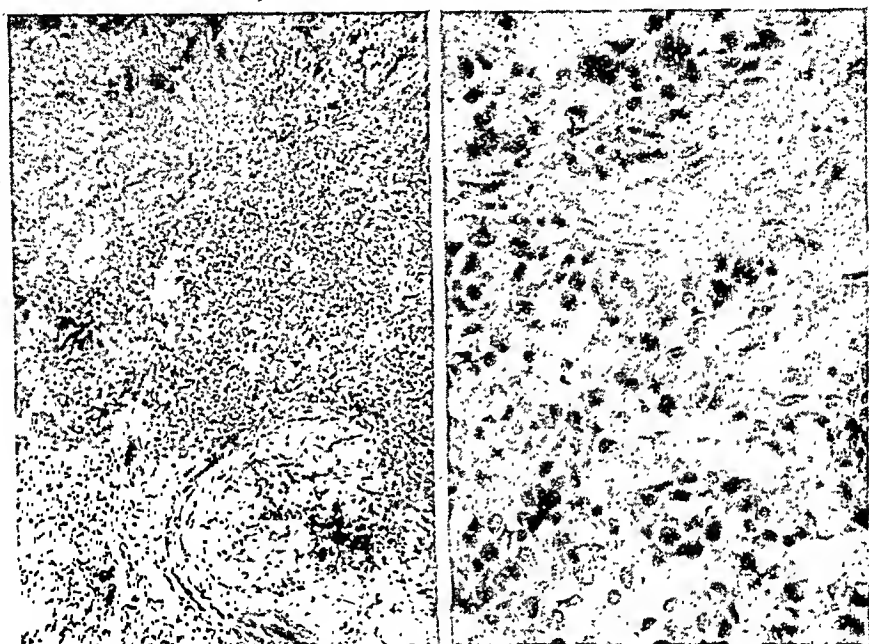


FIG. 1.

Fibro-myxo-epithelioma of benign type from the lacrimal gland of a man, aged 25 years (case 98), where the general picture (to the left) shows the heterogeneous structure with alveolar epithelial cell groups and fibrillar tracts, while the increased magnification (to the right) reveals intracellular myxoma formation and myxomatous degeneration.

or malignant. Often there occur transitional forms, and even different phases within one tumour, so that the differential diagnosis may be difficult or impossible to make. The benign fibro-myxo-epitheliomas are characterized by copious mucus formation and an intact capsule (Fig. 1), whereas the malignant form presents a greater abundance of cells, polymorphism, numerous mitoses and metaplasia, as well as penetration through the capsule.

The basaliomas, whose name is due to the histopathological resemblance to the basal cell cancer of the skin, differ biologically very much from the torpid skin cancer by being highly malignant.

The basaliomas have a cystic and a solid form, which may both be benign as well as malignant. The cystic forms, called also cylindromas, present well-pronounced, mucus-filled cavities surrounded by from 1 to 5 layers of cubic cells (Fig. 2). The solid forms are richer in cells and the cavity formation minimal or absent. The cylindromas are highly malignant despite inconsiderable nuclear atypia and polymorphism. The same has been

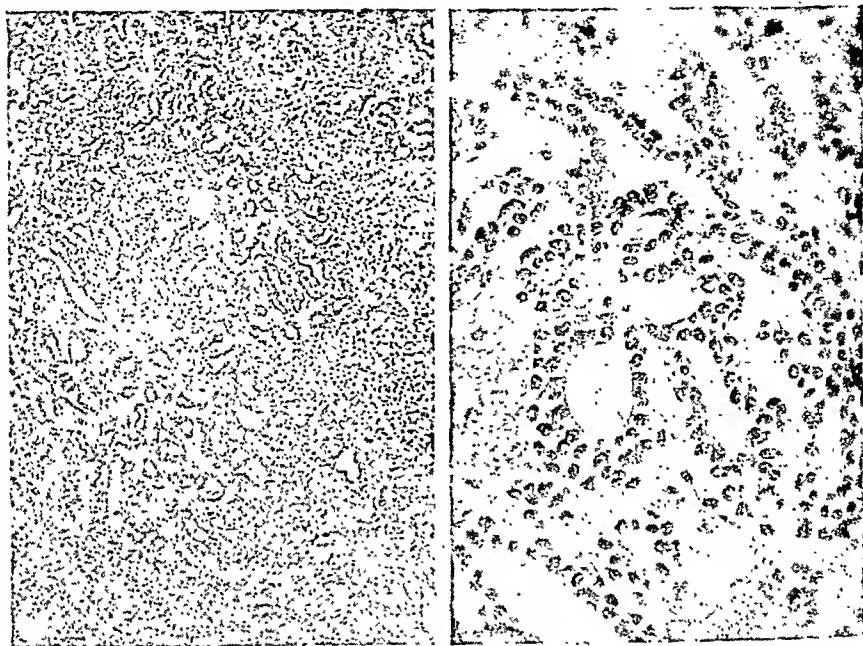


FIG. 2.

Cystic basalioma (or cylindroma) of malignant type from the lacrimal gland of a man, aged 36 years (case 106), where the general picture (to the left) shows a structure rich in cells with multiple alveoli with cavities seen (in increased magnification to the right) to be filled with myxoma and surrounded by 2 to 4 layers of cubic cells with strikingly little nuclear atypia.

observed, though rarely indeed, in other tumour forms (chondromas, plasmocytomas, etc.).

Fibro-myxo-epitheliomas occur more frequently (Ringertz 62 per cent., Ahlbom 73 per cent.) than basaliomas (Ringertz 33 per cent., Ahlbom 17 per cent.). Malignant cases are more frequent than benign. Infiltrative growth and metastases were observed more often by Ahlbom (33 per cent.) than by Ringertz (15 per cent.). The incidence of recurrence was found to be 40 per cent. (Ringertz).

The principles of treatment consisted mainly in operation and irradiation, either separately or combined. The results were best in the cases of nasal and paranasal tumours, where Ringertz found a 5-year-cure-rate in 50 per cent., while Ahlbom found a 5-year-cure-rate in 25 per cent. of his cases of tumour in the large salivary glands. The radio-sensitivity corresponded to that of squamous cell carcinomas of low differentiation. In particular the cylindromas were radiosensitive.

### Own investigations

The present investigation was based on cases of mixed tumours in the lacrimal gland observed in the Eye Department of Karolinska Sjukhuset, Stockholm, within the 15-year-period 1932-46. 78 cases of orbital tumour were admitted within this period, of which 52 were verified as proper tumours, while 5 histologically were pseudotumours, and 21 not verified. Of the 52 proper orbital tumours 36 were primarily orbital with the following points of origin: most often the lacrimal gland (18 cases, of which 10 mixed tumours and 8 lymphomatosis cases); next followed the nerves—including the optic nerve (8 cases), the skeletal parts (6 cases); more rarely vascular elements (3 cases) and dermoid cyst (1 case). (For further particulars concerning this series *vide* Godtfredsen, 1947.)

The data of the 10 cases of mixed lacrimal gland tumour appear from Table 1, on which no detailed comments will be made. Only it should just be mentioned that exophthalmos (6 cases) predominated among the initial symptoms, while visual impairment (2 cases), ptosis, and metastatic cervical glands (1 case each) were rarer. On admission there was in each case found a from pea- to almond-sized palpable tumour in the lacrimal gland of a semi-solid or hard consistence with varying nodular surface. The exophthalmos ranged from 2 to 13 mm. (Hertel). The visual impairment (in 7 patients) was often considerable, without or with attending ophthalmoscopically ascertained choked disc (2 cases) or stasis of retinal veins (1 case). X-ray-verified bone destruction was ascertained in only one of 7 examined cases (localized in the orbital apex). Metastatic lymphatic glands were found in 3 cases, partly preauricularly (1 case) and partly in homolateral cervical glands (2 cases).

Histopathological diagnoses were made partly on biopsy samples, and partly on totally excised tumours, and special staining was carried out to the necessary extent. All the preparations were revised. Histopathological distribution, fate of patients, results of treatment, etc., will be discussed below.

TABLE I. 10 cases of mixed lacrimal gland tumours.

No.	Sex Age	Symptoms, nature, durat. (mths.)	Ophth. find.		Histopath. diagnosis.	Treatment	Course
			Exophthalmos in mm.	Vision			
6	M 51	Exophthal. (36) Loss of vis. (3-4)	10	0.4	Fibro-myxo- epithelioma (benign) do.	Krönlein	?
15	M 54	Exophthal. (24)	10	0.1	do.	Krönlein + radium	Symptom-free 24 months
95	M 22	Exophthal. (24)	2	1.0	do.	Krönlein	Symptom-free 36 months, then loc. recurrence
98	M 25	Ptoxis (18) Exophthal. (4)	3	1.0	do.	Excision + X-rays	Loc. recur. 2 months later dis-app. to repeated treatm. Now sympt.- free 18 months
66	M 23	Cerv. gl. (48) Exophthal. (8)	9	0.4	Fibro-myxo- epithelioma (malignant) Basalioma cystic	X-rays	Progression. Died within 8 mths.
26	F 58	Exophthal. (36) preauric. gl. (1)	6	0.2	do.	1) X-rays 2) Evisc.	Temp. symptom-free 14 months. Loc. recur. Died after 2 mths. Autopsy. Metast. to brain
105	F 38	Exophthal. (3)	8	0.5	do.	X-rays + evisc.	Symptom-free 4 months
106	M 36	Loss of vis. (12) Exophthal. (1)	7	0.1	do.	do.	Symptom-free 12 months
89	M 74	Loss of vis. (?) Cerv. gl.	12	perc. of light	Solid basalioma	1) X-rays 2) Evisc.	Temp. sympt.-free 36 mths. after X-rays. Then recur. Evisc. Died 2 months later
18	F 72	Exophthal. (11)	7	1.0	Basalioma? Sarcoma?	Evisc. + radium	Temp. sympt.-free 24 mths. Then pleurit. Died 27 months after treatment

### Discussion

Although the present series of mixed lacrimal gland tumours is fairly small it possesses certain advantages over those collected by Warthin, Lane, a.o., the present series being homogeneous with regard to revising histopathological estimation and principles of treatment. The patients were furthermore followed up in accordance with the follow-up system of *Radiumhemmet*. The histopathological estimation was made on modern principles indicated by Therkelsen, Ahlbom, and Ringertz. Accordingly a comparison with the experiences of these writers concerning extra-orbital mixed tumours is very perspicuous.

Of the orbital tumours, constituting about 1 per cent. of the cases admitted to eye departments of any size, only one-eighth are mixed tumours in the lacrimal gland (10 out of 78 cases in the present investigation). These latter tumours constitute an even smaller proportion of the entire number of mixed tumours ( $\frac{1}{2}$  to 1 per cent. according to Therkelsen and Ahlbom).

Histopathologically my own 10 lacrimal gland tumours were distributed like the extra-orbital mixed tumours (Ahlbom, Ringertz), 5 being fibro-myxo-epitheliomas, one of which was malignant, and 4 (perhaps 5) basaliomas, of which 3 were cylindromas and all were malignant. In one case the differential diagnosis between basalioma and sarcoma of low differentiation was uncertain.

The incidence of malignant cases on the basis of histopathological criteria (6 out of 10 cases) corresponds to that indicated by Ahlbom (60 per cent.) and Ringertz (72 per cent.), but does not accord with the biological malignancy. From a biological point of view nearly all lacrimal gland tumours are malignant, since the tumour proliferation or the resulting exophthalmos has a deleterious effect on the optic nerve and/or retinal vessels. The vision was unaffected in 3 cases only. Recurrence despite histological benignity occurred in two cases (2 and 36 months respectively after the treatment).

A comparison between the clinical data of the present 10 cases of mixed lacrimal gland tumours and the symptomatology of the extra-orbital mixed tumours shows a rather close accordance with regard to length of past history, age incidence, regional lymphatic gland metastases, and frequency of recurrence.

Although the lacrimal gland tumours are rather superficial and fairly easy of access for both surgical and radiological treatment, the results of treatment are poor. Despite tumour excision with or without irradiation, only 5 of the present 10 patients were found alive, one with recently ascertained recurrence, and the others after

fairly short periods of observation (4 to 24 months). Two of these 5 cases were histo-pathologically malignant.

The tendency of the tumours to spread appears from the fact that distant metastases were observed in two of the deceased, malignant cases (brain and lungs).

Three of the deceased, malignant cases showed that malignant tumours may be radiosensitive, since irradiation brought about freedom from symptoms for from 14 to 36 months.

In point of prognosis the lacrimal gland tumours resemble the large salivary gland tumours (notably the parotid tumours), where the prognosis is worse than for tumours proceeding from glandular elements in the mucous membranes of the nose and paranasal sinuses (5-year-cure-rate for 25 per cent. and 50 per cent. respectively). That the lacrimal gland and the parotid gland as the only purely serous tubulo-alveolar glands of the body also present pathological points of resemblance is perhaps due to the parallelism in anatomical structure.

### Conclusion

The mixed lacrimal gland tumours were previously regarded as histologically and biologically very polymorphous tumour forms. However, the present investigation, based on modern histological criteria, shows that the morphology is simple and that the lacrimal gland tumours resemble, histologically as well as biologically, mucous and salivary gland tumours in other regions, both those in the large solitary salivary glands and those proceeding from mucous membrane elements (Therkelsen, Ahlbom, and Ringertz).

After a clinical diagnosis of lacrimal gland tumour, the symptomatology of which is often simple, it is necessary to have the nature of the tumour ascertained as soon as possible by histological examination of a biopsy specimen, the result of which is decisive for the principles of treatment. If microscopy shows the tumour to be a basalioma it is practically always malignant, whereas the fibro-myxo-epithelioma is most often benign. Biopsy should be omitted only in obviously malignant cases (metastases, bone destruction).

The principles of treatment, settled in concert with *Radiumhemmet*, are as follows: for benign tumours excision either by Kroenlein's operation or by anterior orbitotomy, and for malignant tumours pre-operative X-ray treatment (4-5,000 r.), and 1 month later evisceration of the orbit. Evisceration should not be omitted even if the tumour responds favourably to irradiation (as in 2 of the present cases), because the chance of recurrence is great. Both of the above cases relapsed promptly.

Despite the poor results of treatment in the present series it must be emphasized that more exact diagnosis (biopsy of all suspicious tumours) as well as intensified and earlier instituted treatment would no doubt improve the chances for these patients. The histopathological and biological parallelism demonstrated here between mixed tumours in and outside the lacrimal gland suggests that it should be possible to bring the results of treatment to the same level.

### Summary

The literature on lacrimal gland tumours (most of it casuistic or compilations) is not up to date regarding modern histological classification. The biology and modern histological aspects of extra-orbital mucous and salivary gland tumours are briefly summed up. Next a comparison is made between these tumour forms and the lacrimal gland tumours of mixed type. (Own investigations from 10 cases histologically revised and followed-up.) It appears that there is a pronounced parallelism both histopathologically and biologically.

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## A CASE OF SYMPATHETIC OPHTHALMITIS OF UNUSUAL ONSET RESPONDING SATISFACTORILY TO TREATMENT\*

BY

ALAN W. SICHEL and J. G. LOUW

CAPE TOWN

A. J. v. T., a European farmer, aged 54 years, sustained an injury to his right eye while chopping wood on December 14, 1945, the eye being struck by a large chip which caused it to bleed with immediate loss of sight in it. He consulted a doctor some 16 miles from his farm who examined the eye with a torch, the light of which could be perceived with the injured eye. He was admitted to the local hospital, where he received a course of prophylactic sulpha drug treatment and hot applications over a period of 10 days. The eye was painful on and off and he was advised to have it removed, but this he declined. After returning to his home he decided towards the end of January, 1946, to consult an ophthalmologist in a neighbouring town. As a result he was given drops to use in the injured eye and told that he did not require glasses. According to his statement he could read the smallest letters on the chart when being examined on that occasion, from which it may be assumed that visual acuity in the uninjured eye was 6/6 approximately.

The pain and redness in the right eye gradually subsided but the left eye began to give trouble in the shape of occasional pain, though vision in it was unimpaired. He again saw his family doctor, who advised him to proceed to Cape Town and gave him a letter of recommendation to the Groote Schuur Hospital, where he was admitted on March 10, 1946, under the care of one of us (A.W.S.). In his letter his doctor stated that he feared sympathetic inflammation had set in and that the injured eye would have to be enucleated. On admission, apart from the loss of sight in the right eye, his only complaint was slight watering of the left eye.

*Condition on examination.*—The right eye showed a healed, vertical, linear wound of the cornea involving almost its entire width, but without incarceration of the iris. The pupillary area was occluded by a massive organised exudate. Ciliary injection was considerable while the globe was soft on palpation and very tender to pressure, especially over the ciliary region. Vision in it was reduced to questionable perception of light. The left eye

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appeared normal and vision in it was 6/9. The pupil was regular in contour and reacted briskly to light, the fundus was healthy and there was no evidence to suggest sympathetic ophthalmitis except the complaint of watering already mentioned.

Enucleation of the right eye was advised and performed on March 14 under general anaesthesia. During convalescence the patient complained of watering and evinced slight irritability in the left eye, but examination disclosed no evidence of organic disease. The result of a differential blood count on March 23 was : polymorphs 59 per cent., lymphocytes 36 per cent., large mononuclears 5 per cent. -

On March 25 irritability of the left eye was still evident but slit-lamp examination revealed no sign of iritis; there was no "k.p." and the aqueous was devoid of cells. Vision was 6/9. On ophthalmoscopic examination, however, the presence of mild papillitis was noted, this being the first clinical sign of abnormality since the original injury to the fellow eye some 3 months previously.

On April 1 the patient complained of mistiness of vision which had now fallen to 6/18. Under mydriasis the first evidence of posterior synechiae appeared, together with pigment deposits on the lens capsule, and fine "k.p." was observed in the lower segment of the cornea. Vigorous treatment was instituted without delay. This consisted of 200,000 units of penicillin in 10 intramuscular injections at 3 hourly intervals, together with 0.3 grm. of nearsphenamine by intravenous injection followed 2 days later by a further dose of 0.45 grm. Co-incidentally sodium salicylate was exhibited by the mouth in massive doses, the dosage being scaled at 1 gr. per lb. body weight of the patient during each successive 24 hours.

On April 8 vision was still 6/18. The pupil was well dilated under atropine, papillitis and vitreous haze were noted, but the "k.p." had cleared up to a considerable degree. Owing to a complaint of singing in the left ear the patient was referred to the Ear, Nose and Throat Department. The consequent report offered an explanation for the occurrence of tinnitus which had no bearing on the eye condition and disclosed no evidence of sinus infection. The tinnitus, it should be noted, had existed prior to the administration of salicylates.

On April 11 a full course of sulphadiazine was commenced, treatment by sodium salicylate being continued. The papillitis had become more intense and the vitreous haze denser. Cerebrospinal fluid obtained by lumbar puncture—pressure 190 mm.—was submitted for examination and the report received indicated as

follows : " Clear fluid, colourless and no clot. No cells or organisms seen and no growth on culture. Protein 35 mg. per cent. : Globulin, minute trace : 44 lymphocytes, 6 polymorphs."

On April 15 the eye was painful and some corneal oedema present. The intra-ocular pressure was raised, being 60 mm. by Schiötz tonometer. Atropine was discontinued. In order to relieve the pain and to promote an interchange of aqueous a paracentesis was performed on April 18. Seven days later the condition of the eye was noted as more comfortable and the intra-ocular pressure recorded was 25 mm. Schiötz.

On April 28 the Wassermann, Kahn and Rappaport blood tests were reported negative. Vision was still 6/18 and slit-lamp examination showed fine deposits of pigment on the lens capsule and only one or two minute but not recent deposits on Descemet's membrane. On May 2 a further course of penicillin was given, 800,000 units being spread over 20 intramuscular injections at intervals of 3 hours. Following this the patient was given mist. potass. iodide and for local instillation drops of dionine 4 per cent. were ordered twice daily. The eye remained free from pain and redness until May 25, 1946, when, at his urgent request, the patient was allowed to go home for domestic reasons but on the understanding that he would return as soon as possible.

On re-admission on June 10, 1946, the condition of the left eye was noted as follows : Vision 6/12, corrected by -0.75 D.Sph. to 6/5 : no complaint of pain or mistiness of sight : tension 23 mm. Schiötz. Slit-lamp examination : aqueous clear, one or two fine pigmented deposits in the lower segment of Descemet's membrane. Despite the presence of synechiae the pupil reacts to light. Ophthalmoscopic examination : slight swelling of the papilla and haziness of the vitreous, but notwithstanding vision is 6/5. The patient was provided with suitable glasses and allowed to return to his home without further treatment. He was instructed to return in 3 months' time for further observation.

On September 30, 1946, he returned to the Groote Schuur Hospital as instructed and on examination the condition of the left eye was recorded as follows : Vision with correction 6/5, and with addition for near vision reads J.1 at 25 cm. : slight redness of the bulbar conjunctiva, but no complaint of pain or tenderness on pressure. Fundus : the papillitis has subsided, the disc is slightly pale but its edges are sharply defined and the physiological cup present ; there is slight dilatation of the retinal veins and a suspicion of vitreous haze. Slit-lamp examination shows the anterior chamber to be well formed, the aqueous clear and the pupil, almost circular in shape, to react to light though not briskly ; there are

fine pigmented deposits on the lens capsule and one or two pigmented particles on Descemet's membrane. The intra-ocular pressure is 20 mm. by Schiötz tonometer. The visual field is unimpaired.

The patient expressed himself as feeling like a new man. Whereas while in hospital under treatment he had been low-spirited and anxious about his future, he was now cheerful and without complaint of any kind. He was not detained in hospital but returned home the same day, *i.e.*, September 30, 1946, since when no communication has been received from him or his doctor. From this it can be assumed that he is well and that the condition of his eye continues to be satisfactory.

### Comment

It has been thought worth while to publish this case chiefly on account of the unusual onset of clinical signs indicating sympathetic disease. In the great majority of instances, as any experienced ophthalmologist will agree, the sympathising eye first develops irido-cyclitis of the plastic type with its characteristic changes located in the anterior segment of the globe. In the case under consideration mild papillitis was the first positive indication of an inflammatory process and it was only after a definite interval that signs of anterior uveitis developed. This confirms Duke-Elder's statement "on the other hand, but much more rarely, the disease may start in the posterior segment without evidence of an irido-cyclitis but with swelling and congestion of the optic nerve and diffuse retinal oedema most marked at the posterior pole."<sup>1</sup>

The infective theory of the pathogenesis of sympathetic disease is the one which up to the present finds most support and this case suggests that the path of infection from the injured to the sympathising eye may well be *viâ* the optic nerves and chiasma, that is to say by the anatomical route.

As regards the response to treatment it is difficult to assign the credit to any one of the methods employed. Indeed it has been pointed out by some observers that the milder types of the disease may clear up even without any special type of treatment; possibly in this case the disease was of a mild nature. It may be, however, that penicillin, not available when treating previous cases of sympathetic disease at the Groote Schuur Hospital, played the principal part in saving the eye.

### Summary

A case of sympathetic ophthalmitis is reported in which the first sign of the disease in the sympathising eye was a mild papillitis occurring 3 months after an injury to the fellow eye.

Intensive treatment, including besides local measures penicillin, sulphadiazine and massive doses of sodium salicylate, led to a satisfactory result being obtained. It is possible that penicillin, from the therapeutic standpoint, played the most important part.

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## AN EYE SPECULUM WITH DIFFERENT BLADES FOR UPPER AND LOWER LIDS\*

BY

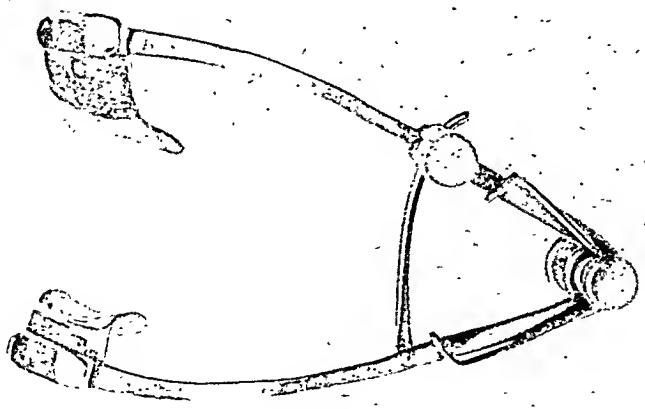
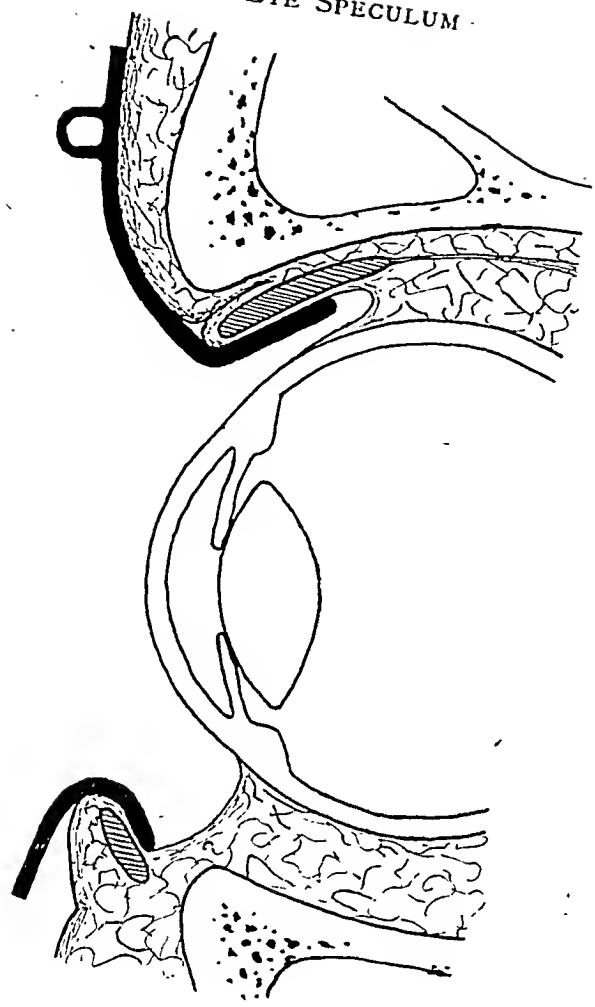
B. S. HYLKEMA

ASSEN, THE NETHERLANDS

ALTHOUGH the upper and lower eyelids differ considerably in form and in their relation to the surrounding tissues, in the eye specula commonly used the wire loops or blades which hold the two eyelids apart, are of the same shape. The tarsus of the upper lid is broader than that of the lower. It is, moreover, connected with the levator palpebrae superioris muscle whereas there is no similar muscle in connection with the lower tarsus. Consequently the lower lid has a great passive mobility and can be easily pulled downward and a little forward, into a position convenient for the operation. For this reason the lower loop or blade of the speculum should be of such a form as to retract only the lower lid and must therefore be rather sharply bent which, as a matter of fact, is also the case with the usual specula. The mobility of the upper lid, on the other hand, is much more limited. It can be raised only in a direction parallel to the surface of the eyeball bringing the tarsus between the roof of the orbit and the globe. Were this movement to be carried out by means of a loop or blade curved to the same degree as that for the lower eyelid, it would hit the supraorbital margin before the tarsus had been brought completely within the orbit. This difficulty is overcome by a loop or blade with wide curve taking in both the supra-orbital margin and the tarsus.

For holding the eyelids apart curved metal blades are preferable to wire loops. A blade severs the margin of the eyelid from the field of operation thus promoting sterility. Moreover, the pressure and stretching suffered by the eyelids from a blade are less than by using a loop, as a result of which the patient feels less of the instru-

\* Received for publication, September 9, 1947.



ment, this contributing to a calm and easy procedure of the operation. In order to obtain the greatest possible adaptation to the anatomical relations these blades must be bent in the shape of a saddle while in addition the upper blade must have an arch parallel to the surface of the eyeball.

In cataract operations any pressure from the instrument upon the eyeball must be avoided. In the case of the lower blade there is no danger of this as it is kept at a safe distance from the globe. In the case of the upper blade, however, this danger does exist, even if the exerted pressure is slight, this blade being supported by the rim of the orbit. To avoid this pressure on the eyeball the upper blade is provided with a small curved piece of wire. Through the eyelet, thus formed, a thread can be passed if necessary which can be held tight by the assistant at the operation to prevent the metal coming into contact with the eyeball. - This can be performed by one less experienced in eye operations.

If a speculum with dissimilar blades is to be employed for operations on the right eye as well as on the left, the blades should not be attached to the instrument. On the speculum illustrated here, the blades can be detached from the arms and alternated. A spring prevents them from slipping off easily.

The hinge of the instrument has an adjustment screw which rests against the patient's temple. By means of this screw this part of the speculum can be slightly tilted to improve the adapting of the blades to the eyelids.

The instrument, as illustrated, has been tested upon several people and has been put into practice in various kinds of operations. It has been shown that by its use a very wide palpebral fissure is obtained, while according to those tested, they felt no pressure on the rim of the orbit; at the most, slightly the stretching of the external canthus.

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## USE OF POLARIZED LIGHT IN SCOTOMETRY. WITH BINOCULAR FIXATION

BY

ULF HALLDÉN

UPPSALA

A GREAT number of different devices have been constructed to allow of the investigation of the visual field using binocular fixation. In ordinary cases binocular fixation will be somewhat more steady than monocular, but the difference is hardly of practical importance. In

all kinds of central scotomata, however, (retrobulbar neuritis, macular changes and similar conditions) the monocular method is insufficient. In most cases of concomitant strabismus without amblyopia, there are as Harms (1937), Travers (1938) and others have shown, transitory scotomata which disappear immediately when the eye not under investigation is occluded. Those scotomata can only be studied with the binocular method.

Haitz in 1904 introduced his charts which were to be observed with an ordinary stereoscope. He utilized only a ten degree field, a disadvantage especially in the investigation of squint. An important improvement was made by Lloyd (1920) and his instrument in its numerous modifications seems to be widely used, especially in the U.S.A. It is generally preferred, however, to make the campimetric investigation at a distance of one or two metres. To this end Harms (1937) used red-green glasses and as a test-object, a red disc, invisible through the green glass. The use of a coloured test-object to investigate the field for white, seems rather unnatural. Foster (1938) has described an ocular with a mirror reflecting a fixation light placed outside the screen, and Travers has used a mirror in his investigation of the nature of suppression in squint. It must be a laborious and time wasting procedure to adjust the mirror, at least in cases of squint.

If a beam of polarized light is projected on to an aluminized screen, it is reflected irregularly, that is without glare, but with very little change in the polarization. The projectors described by Juler (1939) or by Odqvist (1942) may be adapted for the purpose, by attachment of a polaroid filter. I have myself used the Odqvist projector. The screen is viewed through polaroid filters with the planes of polarization at right angles to each other. By rotating the polarizer it is possible to extinguish the projected spot of light for the eye not under investigation, while the point of fixation and the whole screen are simultaneously fully visible for both eyes. The projected spot of light is now used as a test-object for the campimetric investigation. In this way it is easily possible to examine the visual field, within the limits of the tangent screen, at any distance from one to four metres, with a very free choice as to diameter and contrast of the test-object, and to use colours as well as white.

On the usual Bjerrum screen of black cloth the limits found are temporarily marked off with pins. This is not possible with an aluminized screen, I have used a screen of aluminized sheet iron, and small permanent magnets as indicators.

A grant from the Swedish Society for Medical Research is gratefully acknowledged.



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 ANNOTATION
 

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## When not to operate

It is not easy to lay down precise rules on this subject. Most of us formulate our own. Speaking generally no surgeon is bound to undertake an operation if, in his judgment, the risks are too great, or the benefit therefrom too problematical. The patient is always free to consult somebody else, if he is not satisfied. Nobody disputes that cases of acute glaucoma or perforating wound with iris prolapse must be operated on. In ophthalmology it is in cases of cataract that the question of when not to operate mostly arises.

In pre-insulin days most of us were chary of undertaking an extraction of cataract in diabetics. But, nowadays, with the diabetes controllable, the problem hardly arises. We always considered that unilateral cataract with good vision in the other eye was for the most part best left alone. Particularly in cases of cataract with precipitates on the cornea we should not be too ready to suggest operation. It is often said that when a patient is practically blind with double cataract, he can hardly be made worse by an operation and he may be made very much better; and in general we agree. But, even so, there are times when things do go wrong, the eye does badly and has to be removed.

We recall a couple of cases of our own bearing on this point. In one we refused to operate, in the other we consented. The latter case was a labouring man with double cataract and insufficient sight to enable him to do his work. In addition to cataract he had every indication of having had trachoma in his youth and he had also had iritis as evidenced by posterior synechiae. We decided to do an iridectomy in the first instance to see how the eye would react, but before we could do it we had to do a canthotomy to get the speculum inserted. The eye did well; the lens was extracted at a second operation, the capsule finally needled, and vision of 6/9 made the man quite satisfied.

The other case was in a man, aged nearer 90 than 80, whom we were asked to see soon after we started practice. He had only one

eye, the other had been lost after a cataract operation about ten years earlier. This case was a typical one in which not to operate. The cataract was hypermature, of a very nasty colour, with capsular thickenings. The iris was muddy and atrophic; posterior synechiae were present. We could not find any precipitates and the projection of light was very poor. In spite of the prayers of his doctor and himself to do something we refused to have anything to do with it.

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## FACULTY OF OPHTHALMOLOGISTS

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### Report of Council Meeting on January 9, 1948

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THE report of the Joint Sub-Committee of the B.M.A. Ophthalmic Group Committee and the Faculty on the Future of the National Ophthalmic Treatment Board was discussed. The Council agreed that the continuation of the N.O.T.B. in the Supplementary Service should be supported and approved the report except in so far as they did not feel it was advisable that the N.O.T.B. should infiltrate into hospitals and use hospital clinics as premises if these premises could be used for clinics under the Permanent Service.

A memorandum on the Ideal School Ophthalmic Service, prepared for the Ophthalmic Group Committee by Mr. Black and Mr. Mackie, was approved with minor amendments.

The Council approved the memorandum on "Ophthalmology in Industry: a pilot experiment," prepared by Mr. Duthie, which it was proposed to carry out in Manchester in association with the University of Manchester and the Eye Hospital.

With regard to the study visits to clinics abroad, the Council agreed that the selection of applicants should be left to the discretion of the Sub-Committee, but suggested that preference should be given to junior Members, of the status of assistant surgeon.

A query as to what conferred on Orthoptists the right to practise had been referred to the British Medical Association, who had replied saying that if an Orthoptist transgressed rules, ethical or otherwise, which, in the opinion of one or all of the sponsoring bodies made it undesirable for her to practise under their aegis, the body whose rules had been infringed was the body to expel the offender from membership, and that expulsion by the Orthoptic Board would carry with it deletion from the Register of Medical Auxiliaries.

It was reported that an objection to the increased fee of 2 guineas,

which was now operating where insured persons were referred by ophthalmic opticians to ophthalmic surgeons, while at the same time ophthalmic surgeons were prepared to see insured patients sent direct by the Approved Society for a fee of 1 guinea, had been referred to the B.M.A. Ophthalmic Group Committee, who had reaffirmed its opinion that the increase should be made. This was endorsed by the Council.

The following resolutions put forward by the Medical Staffs and Matrons of the Ophthalmic Hospitals regarding the Working Party Report on the Recruitment and Training of Nurses were approved:—

(a) Ophthalmic nursing should be acknowledged as a specialty. It should not be considered part of the training for general surgery but should be carried out in a separate unit or complete department controlled by a specially-trained sister, or in her absence, by a specially trained staff nurse.

(b) Nurses desiring to specialise in this work should be sent to an ophthalmic hospital where possible, otherwise to the eye unit in a general hospital for their intensive training, to be followed (if they still wish to continue in this branch), by one year as a staff nurse under supervision.

It was agreed to recommend that the ophthalmic hospitals should continue to be able to recruit applicants to nursing at an age earlier than 18. The Honorary Secretary was requested to forward these resolutions to the Ministry of Health, communicating the Council's agreement and support.

The B.M.A. Ophthalmic Group Committee's recommendation that, pending the examination, agreement and approval of curricula by the representative bodies of the profession and opticians, medical practitioners should take no part in the instruction or examination of opticians or student opticians in clinical ophthalmology, was approved.

A request had been received from the National Institute for the Blind for copies of technical periodicals to be sent to ophthalmologists in the British Zone of Germany. The Honorary Secretary was instructed to draw special attention to this in this summary of the Council minutes in the Medical Press, asking ophthalmologists to send any periodicals they could spare to the National Institute for the Blind, 224-6-8 Great Portland Street, London, W.1.

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CORRESPONDENCE

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PERIPHERAL AND CENTRAL DISTURBANCES OF  
THE VISUAL FIELDS. AN ASPECT OF  
DI-OPHTHALMOLOGY

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—Although Dr. N. A. Stutterheim is to be congratulated upon the success of his treatment in the three cases he describes, tiring and laborious though it must have been both for doctor and patient alike (83 sessions for the first case, 43 for the second and 21 for the third), one cannot help feeling that equally satisfactory results might have been obtained by a variety of other methods of surgery.

In spite of the negative "neurological" reports in Cases 1 and 2 (no such report is given in Case 3) any impartial reader with a mere nodding acquaintance with the elements of neuro-psychiatry must, after studying the clinical data relating to these cases, come to the conclusion that a psychogenic basis for the symptoms described is more than probable. It must, of course, be admitted that convergence insufficiency is a common finding in ocular psycho-neurosis, and further that such a defect is amenable to treatment by means of exercises. Moreover, if such a defect is associated with other "functional" visual anomalies, its cure by a sufficiently persuasive practitioner may lead to the cure of the associated visual anomalies also. But from the results of such therapy it cannot be concluded, as Dr. Stutterheim has, that the convergence insufficiency was the essential cause of the ocular symptoms.

With regard to Case 3 it would appear that the ophthalmologist who first examined the case was of the "alarmist" type, and as often happens in such circumstances, symptoms which are at first slight soon assume gigantic proportions. This case would appear from the available data to be one of mild spasm of accommodation such as might be rapidly cured by a short course of atropine drops.

As far as the symptom of photophobia (as described in Case 2) is concerned, necessitating the use of dark glasses, one has come to regard a patient who, in the absence of any ocular disease, wears dark glasses, especially if he insists upon keeping them on when he enters the usually dim light of the ophthalmic consulting room, as either a person who is grossly absent-minded or else one who is suffering from photophobia of "functional" origin.

Improvement of visual acuity as a result of convergence exercises

in a case of convergence insufficiency and/or heterophoria is, in my experience, not uncommon, especially in those cases which demonstrate definite ocular neglect or suppression of one eye. But even in cases in which the visual acuity is slightly defective in both eyes (in the absence of organic cause) a course of exercises, by stimulating the patient's visual perception, may improve his visual acuity. In such cases one would expect to find a generalised depression of visual acuity over the entire field which may well be sufficient to cause a slight "contraction" of the peripheral field. This, however, will not explain the gross bilateral field contraction described in Case 1 in the report of the second ophthalmologist given on p. 724 *before convergence exercises were commenced*. His description of the fact that "the patient walked about the place without difficulty, totally unlike a person who had a visual field contraction as is shown on the visual field charts"—can only have one of two explanations—either the visual fields were incorrectly examined or else the patient was an hysteric or a malingerer.

It is a pity that such enthusiasm for a particular form of therapy—a form of therapy indeed of the greatest value in suitable cases, should allow an authority as great as that of Dr. Stutterheim to attach such fantastic labels to cases which are clearly psychoneurotic in origin, and to add such a nebulous term as "dipththalmology" to a branch of medicine which is already overladen with verbose terminology!

I am, Yours faithfully,

T. KEITH LYLE.

42, CHARLES STREET, W.I

January 5, 1948.

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## NOTES

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Chengtu Eye, Ear,  
Nose and Throat  
Society, China

THE Chengtu Eye, Ear, Nose and Throat Society celebrated its tenth anniversary on Dec., 20, 1947. Dr. T. H. Lan, professor of biochemistry, West China Union University, was invited as the guest speaker. He spoke on the biochemistry of blood in patients suffering from malignant tumours. Drs. K. C. Lang and E. Chan reviewed the history and progress of the society during the past decade. A photograph was taken to commemorate the eventful occasion and a dinner party concluded the session.

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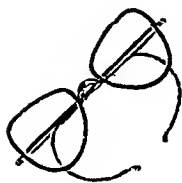
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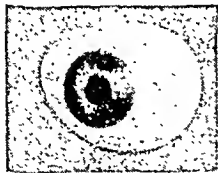
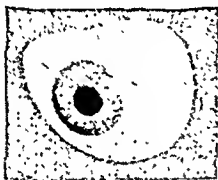
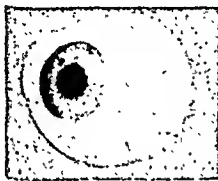
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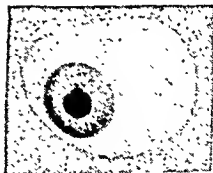
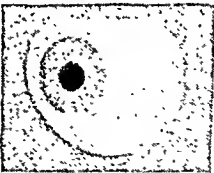
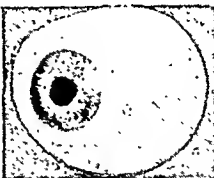
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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

APRIL, 1948

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## COMMUNICATIONS

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### CLINICAL REPORT ON MINERS' NYSTAGMUS\*

BY

DOROTHY ADAMS CAMPBELL

COVENTRY

THIS report is based on my observations on 44 cases of miners' Nystagmus which have been referred for a report, or which came to the Coventry and Warwickshire Hospital during the period June 1, 1945 to May 31, 1947.

Each man has been investigated as to clinical symptoms, and supervision has continued by getting him to attend the hospital clinic at regular intervals, usually once a month.

General treatment has consisted of the prescribing of glasses, where necessary, and the administration of general tonics or vitamins. Orthoptic treatment has been given in a few cases, and a course of rehabilitation exercises was attempted in 12 cases.

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\* Received for publication, November 22, 1947.



Every attempt was made to get the men to return as soon as possible to some form of work (See Table I).

*Miners' Nystagmus — 44 Cases*

TABLE I

Name	Age	Date of Certification	Nystagmus	Giddiness	Photophobia	Blepharospasm	Present Work 1st May, 1947
1947			Symptoms	at first	visit		
E.D.	49	1944	—	—	+	—	Surface
E.H.	52	1943 & 1947	—	—	+	—	Surface
F.P.	39	Prewar & 1947	—	—	—	—	Underground
F.S.	36	1947	+	+	+	—	Off work
1946							
W.A.	45	1946	—	++	++	+	On light wk. surf.
R.B.	42	1945	—	+	+	—	Surf/Powerhouse
A.H.B.	60	1932	...	...	...	...	Surface
S.B.	52	1945/46	+	+	—	—	Blacksmith's mate
T.H.C.	50	1937/40/42	—	...	...	...	Surface
E.F.	44	1931/41	—	—	+	...	Goods Guard
T.D.	31	1946	++	...	...	...	Hotel Porter
N.F.	45	1945	+ L.E.	...	...	—	Chimney Sweep
E.R.	64	1945	—	...	...	...	Off work (age)
A.R.	42	1944	+	...	...	...	Surface
J.H.R.	41	1946	—	...	...	...	Off work
J.S.	72	1946	+	...	...	...	Surface
H.S.	47	1945	+	...	...	...	Surface
T.S.	53	1945	—	...	...	...	Surface
F.S.	43	1 45	occ.	—	—	—	Bank till Mch. 1947
S.A.	71	1933	—	...	...	...	Off work (age)
N.W.	48	1945	+	...	...	...	Labourer
A.W.	46	1946	—	+	—	—	Labourer
E.J.	46	1945	—	—	—	—	Flour packer
1945							
E.B.	47	1941 & 1944	+	+	+	—	Labourer
E.B.	59	1946	+	—	—	—	Surface
J.T.D.	43	1944	—	+	+	—	Surface
S.D.	60	1945	—	+	—	—	Surface
G.E.	58	1946	+	—	—	—	Finished wk. (age)
R.E.	59	1940	—	—	+	+	Watchman (Colliery)
B.H.	64	1943	+	+	+	+	Labourer
W.H.	47	1945	+	—	—	—	Surface
E.M.	57	1943	—	—	—	—	Underground
J.M.	46	1945 & May 1947	—	—	—	—	“ till May, 47
O.	52	1946	+	—	—	—	Surface
P.	50	1943	+	—	—	—	Underground
J.P.	43	1939 & 1946	—	—	—	+	Released
C.P.	34	1945	+	—	—	—	Office (Colliery)
E.P.	45	1945	+	—	—	—	Surface
W.R.	43	1944	+	—	+	—	Still off work
H.T.	48	1942	—	—	+	—	Corporation Emp.
T.	31	1945	—	—	—	—	Factory
T.T.	47	1939	—	—	—	—	Underground
D.W.	47	1946	+	—	—	—	Surface
B.W.	62	1944	—	—	+	++	Surface

For purposes of comparison, a number of "control" miners (42) were also examined. These were men who attended hospital in most instances for a minor eye injury, or for refraction for reading glasses.

In addition, there was a small group (Group 3) of 8 miners, whose clinical symptoms were suspicious of early nystagmus, and a group (Group 4) of 5 miners who were working underground without symptoms, but with active nystagmus. Total number of miners examined—99.

In addition, the men were examined in the Research Department of the Birmingham Eye Hospital by several members of the Medical Sub-committee of the Miners' Nystagmus Research Committee of the Coal Board. It should be noted that the miners appreciated the tests, but it was very necessary to gain their confidence beforehand.

The special tests are described in the accompanying papers. They consist of:—

1. The estimation of "threshold" of dark adaptation. (See Dr. Sharpley's records.)
2. A psychological examination. (See Dr. Stern's records.)
3. Measurements of binocular vision. (a) in full light adaptation. (b) in dark adaptation.
4. Estimations of:—Blood vitamin A. Blood alkaline phosphatase. Test for liver function.
5. Inquiry into the nutrition of miners.

### Clinical survey

Of the 44 certified cases (see Table I) all were off work when I first saw them; 20 showed active nystagmus; in 9, giddiness was the most prominent symptom; and in 12, photophobia. Only 6 showed blepharospasm—and these were psychologically abnormal to the ordinary observer. After coming under medical supervision, the average duration of incapacity before resuming work was six months. A review of the cases on the 1st May, 1947, showed that all but 3 (2 recently certified, and 1 who was psychologically hopeless) had returned to work.

Of the 8 suspected cases of miners' nystagmus 5 continued to work on the coal face, and 1 as deputy on lighted roadways; the other 2 were given surface work, but were not certified.

The 5 cases of nystagmus-sine symptoms were working on the coal face, but 1 of these broke down in May, 1947.

Of 42 control miners—36 were working underground, 3 were

on the surface, 2 released to factory and brickyard, and 1 was an outdoor mine official.

It was interesting to compare my results with the official figures issued by the West Midland Division of 49 compensable new cases of miners' nystagmus which were certified during the year 1946. They included 6 of my own cases—but if these are eliminated the state of recovery of the men who presumably had no medical "follow-up"—is more evident (See Table II).

*Recovery of certified cases of Miners' Nystagmus*

TABLE II

	Total	Not Working	On light work	Under-ground	In other industries
Group 1					
Under Hospital Supervision	44	3	21	5	12
Unsupervised cases	43	22	19	0	2

It is clear that with or without treatment 50 per cent. of the certified cases can return to light work (usually on the surface) within a very short time, *i.e.*, in 1-3 months. With encouragement even the worst cases, if they are not too old, are capable of resuming some form of occupation in an average of six months. (Cf. the period of disablement for those described as "totally disabled" in the official list—is left a blank!) It is surely better for men to leave the mining industry altogether than for them to remain off work indefinitely.

It must be remembered that there are numerous economic factors which encourage a miner to stay off work for a long time unless pressure is brought to bear on him—*e.g.*, work on the surface can be as profitable to him as underground work provided that he remains in receipt of compensation. Further a better selection of light work is required—as the newly certified case cannot easily return to such work as screening, "tippling," loading of wagons, or laying of sleepers, which involve a great deal of stooping.

### Conclusions

As the result of a clinical investigation of miners suffering from nystagmus, I have come to the following conclusions:—

1. The initial system of certification is unsatisfactory, in that:—

- (a) The certifying surgeon is not required to have any special ophthalmic knowledge.
- (b) The present terms for certification are open to criticism.
- (c) A miner with nystagmus, but without symptoms, is often made conscious of this "disease" by his optician or doctor, or even a friend, and is then sent for certification in order that he may get his just compensation. Such a man might continue to work happily underground, particularly if he could be given better illumination.

2. When certified, the miner remains without treatment of any kind—he may not work for many months and continues to draw a monthly certificate. He is only referred to an ophthalmic surgeon when the continuance of compensation comes under question.

3. Cases of miner's nystagmus fall into three grades:—

- (a) Those with actual nystagmus, but no symptoms, who continue to work underground.
- (b) Those who come within the act for certification, who have headaches, photophobia or giddiness, and also complain that oscillation of lights underground prevents them from working.
- (c) Those with psycho-neurosis, who—in addition to the usual symptoms—develop blepharospasm whenever they are subjected to examination.

The lack of treatment and lack of occupation after certification may easily convert a man of grade B into grade C, and cause a further deterioration in patients in group C.

4. It is, therefore, most desirable that:—

- (a) The miner should return to suitable work, *e.g.* on the surface as soon as possible—preferably without an interval of unemployment.
- (b) That his fitness for work and the necessity for certification should be judged at the onset by an ophthalmic surgeon and a psychiatrist, who have special knowledge of the disease.
- (c) When a man is found unfit for work, he should be given initially some form of holiday, and/or, rehabilitation treatment. My experience has shown that the latter, in the form of remedial exercises, is unsatisfactory when conducted in an out-patient department, owing to the difficulty of travelling and the unsteadiness which follows

exercise. \*Residential treatment is therefore recommended, particularly for grade B. It should include general and special physical training, occupational therapy, and psychiatric consultations, together with orthoptic treatment in cases where it is likely to be beneficial.

- (d) In the "follow-up" work necessary in cases of miners' nystagmus, a medico-social worker would be most helpful.
- (e) Some adjustment in the mode and rate of payment of compensation should be made, so as to make a return to work financially attractive.
- (f) A more careful selection of appropriate tasks is required, in order that the miner shall not be required to work in poor illumination and in awkward postures.

Vast sums are spent in the annual payment of compensation for miners' nystagmus. These recommendations are made in the hope of improving the treatment of the disease once it has occurred, and of procuring a state of physical and psychological recovery (see Dr. Stern's paper) which no longer requires compensation. So far, there appears little hope of achieving such a degree of cure as to enable the certified man to return to work underground—without the probability of a relapse within a year or two.

The original reports issued by the Medical Research Council (almost twenty years ago) stressed the need for improvement in working conditions underground—particularly in the matter of illumination. It is true to say that these recommendations have been almost entirely disregarded—and that little has been done to prevent the disease. When one remembers that the average age of certification is 47—and that the disease affects skilled men in the prime of life—every effort should still be made to stimulate the interest of ophthalmic surgeons and management committees in the prevention and cure of this disease.

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\* As from October 1, 1947, through the Miners' Welfare Commission, facilities for residential treatment have been made available at the Miners' Rehabilitation Centre, Higham Grange.

## THE DARK ADAPTATION OF COAL MINERS SUFFERING FROM NYSTAGMUS

BY

FORBES W. SHARPLEY

FROM THE NUFFIELD LABORATORY OF  
OPHTHALMOLOGY, OXFORD

### Introduction

It has long been known that miners suffering from nystagmus commonly exhibit signs of poor dark adaptation.<sup>1 2 3 4 5</sup> Some investigations of the prevalence and degree of night blindness have been made in the past, but in most of these the experimental conditions either do not appear to have been adequately controlled or else are not fully stated. For these and other reasons it was decided to make dark adaptation tests under strictly controlled conditions, not only on men who were obviously suffering from the disease, but also on miners who were not victims and on completely normal non-miners.

### Type of test

It was decided that the simplest possible test giving consistent results should be used, since men suffering from nystagmus are notoriously apt to be nervous and often somewhat dull mentally. For this reason no disturbing initial bright light adaptation was used and only the final rod threshold measured. Fortuitous initial variations in the state of light adaptation due, for example, to entering the dark-room from out-of-doors daylight, were reduced to a minimum by the practice of causing the subject to remain in the room illuminated solely by ordinary artificial light for 15 minutes before completely darkening the room. Repeated tests on control subjects showed that any residual effect on the final rod threshold was entirely negligible. The same subject tested by day and by night gave consistent results.

A further reason for not placing emphasis on any measurements other than the final rod threshold was that it is known that even for normal subjects the course or rate of adaptation varies considerably in different individuals, especially in the early stages of dark adaptation. When a single figure is used for assessing visual performance in the dark, measurements are therefore best made in conditions approaching complete dark adaptation. It is true that a common complaint amongst nystagmic miners is that it takes them longer than usual "to get accustomed to the dark." They do not so frequently complain of inability to see in a dim light

after sufficient time for dark adaptation. Hence, it would have been of interest to measure the rate at which they dark adapt, but simplicity and avoidance of discomfort to the subject were considered of more importance in deciding on the procedure of the test. On the other hand, every effort was made to measure the final rod threshold as precisely as conditions would allow.

### Instrument and method

The dark adaptometer used was a Hecht-Shlaer Model No. 3. This is a portable instrument using a fixation point and arranged to present the test light in short flashes (of one-fifth second). The area of the retina tested is a disc of  $3^\circ$  extent whose centre is situated  $7^\circ$  above the fovea. The test is binocular and the natural pupils are used. The distance between the eye and the test field is approximately 10 inches. Filters are incorporated in the instrument which pass only extreme violet light to the test field. The instrument is so designed that the reading of the brightness scale can be calibrated from time to time in a simple manner by means of a self-contained standard lamp and photometer. Thus, ageing of the working lamp could be compensated for.

The approximate value of the light threshold of the fully dark adapted eye was first found by giving each subject a few flashes of the test light covering a range of brightness from that clearly visible to that quite invisible. This procedure, incidentally, gave the subject some desirable initial practice. Within the ascertained range limits a series of flashes was then given in random order of brightness. After a short interval this series was repeated four times. The final value of the threshold was computed by a statistical method on the basis of all five series, involving altogether some 30 to 45 exposures. All the subject had to do was to say whether or not he had seen each flash. The actual test occupied less than 10 minutes, apart from the initial period of dark adaptation, which was usually 40 minutes, and never less than 35 minutes, and itself followed the 15 minute period in a dimly lighted room, as mentioned above.

The dark adaptometer used was calibrated in log micro-micro-lamberts as brightness units ( $\log \mu\mu$ ). It is known that there is a range of uncertain seeing near the threshold of about one log unit. Within this range the flash will sometimes be seen and sometimes not. The chief cause of the variation in visibility has been shown to be random physical fluctuations in the light source caused by the quantum nature of light.<sup>6</sup> Hence, the necessity for using a considerable number of flashes. From a study of the "scatter" of the results obtained on testing 125

normal subjects (non-miners) it was found that the value of the threshold computed from the results of the five series of exposures could be relied on to give a precision of  $0.1 \log \mu\mu l$  (computed on the basis of three times standard deviation). The first series of exposures used alone would give a precision of about  $0.25 \log \mu\mu l$ . This is substantiated by the results of other workers.

### Normals

A group of 125 subjects (non-miners) used as normals were volunteers of both sexes and various ages. They were not chosen strictly at random. While no conscious choice was exercised in selection, a certain amount of unavoidable selection was introduced by the difficulty of obtaining the necessary volunteers with the time to spare, especially in the higher age groups. It was a matter of accepting those who could come for test, provided they showed no serious visual abnormalities, other than moderate errors of refraction. The majority of the subjects had no scientific training, though a proportion, especially in the younger age groups, was made up of medical students or medical or nursing staff.

The subjects were divided into age groups, each group covering a range of 10 years. A summary of the dark-adaptation measurements is given in Table I.

TABLE I. *Normals (non-miners)*  
Final rod thresholds when completely dark adapted.

Age group (years)	10/20	20/30	30/40	40/50	50/60	60/70
Number of subjects	27	25	31	26	12	4
Average value of threshold ( $\log \mu\mu l$ )	>1.75	1.86	1.94	2.07	2.15	2.23
Standard deviation of threshold values	—	0.23	0.20	0.32	0.27	0.32

In the case of the 10/20 years age group it was found that a number of subjects showed a threshold below the lowest value measurable with the adaptometer used. For this reason and because no miners in this age group were examined, the results for this group have not been so far utilised.

The continuous increase in the threshold value with age is very evident and confirms that found by other workers.



In order to obtain some estimate of the variability of the threshold for the same subject as measured on different occasions, one subject was given eight complete repeat tests at separate sittings at intervals of a week or two. The results are given in full in Table II, which shows not only the threshold as computed on the basis of all five series of exposures of the test light, but also that based on the first series, first two series, and first three series alone. The decreasing scatter of the computed threshold values for increasing number of exposures of the test light is of interest. Repeated tests on several other subjects (not here recorded) show similar characteristics in general.

TABLE II. *Normal (non-miner)*

Final rod threshold when completely dark adapted.  
Repeated tests on one subject.

Test No.	Threshold in log $\mu\mu$			
	1st exposure series alone	1st two series alone	1st three series alone	All five series
1	2'35	2'35	2'29	2'27
2	2'25	2'30	2'29	2'29
3	2'05	2.20	2'19	2'21
4	2'25	2'20	2'25	2'25
5	2'25	2'30	2'32	2'31
6	2'10	2'20	2'21	2'17
7	2'25	2'25	2'25	2'27
8	2'35	2'25	2'29	2'29
Mean	2'23	2'26	2'26	2'26
S.D.	0'107	0'056	0'045	0'047

Confining attention to the values in the last column for all five series of exposures (which are comparable with all the other results in this report) it will be seen that the variation of threshold as found at different times is not large. Part of the difference is

no doubt real and due to physiological factors. The same factors may be expected to affect the results of all subjects tested, to an extent of the order shown for the same subject on different occasions. Compared with the actual differences between individuals (as shown in Table I above for normals and in Table III for miners) this variation is seen to be in general negligible.

### Miners

A total of 76 miners were tested at the Birmingham Eye Hospital in the following groups:—

	subjects
Group (a) certified cases showing active nystagmus ...	17
Group (b) certified cases showing no active nystagmus	22
Group (c) not certified, but exhibiting active nystagmus	4
Group (d) not certified, and showing no active nystagmus, but suspected early cases ...	6
Group (e) not certified and showing no nystagmus or other symptoms (control group) ...	27
Total Subjects	76

Most of the men came from pits in the Coventry and Warwickshire areas. They had been under observation by Dr. Dorothy Campbell at Coventry or Birmingham and the classification for each case was decided by her. In the case of those men certified for nystagmus, periods varying from months to years had elapsed between certification and date of dark adaptation test. The results of the dark adapted threshold are given below.

TABLE III. *Miners*

Group	Number in group	Number effectively tested	Average age	Dark adaptation mean (after individual correction for 40/50 age group)	Standard deviation
(a)	17	15	47.2	2.30 log $\mu\mu$	0.25
(b)	22	21	49.0	2.56    „	0.52
(c)	4	4	48.5	2.56    „	0.24
(d)	6	6	43.8	2.32    „	0.59
(e)	27	27	44.8	2.34    „	0.44

The threshold figures shown are each directly comparable with The figure of  $2.07 \log \mu\mu$  given in Table I for normals (non-miners) in the 40/50 age group. As such a large proportion of the miners tested fell into this age group it was decided to adjust all results to this basis. This was done for the individual results of all miners falling in other age groups by adding to or subtracting from the actual test result the difference between the mean value for normals (non-miners) in the 40/50 age group, *viz.*  $2.07 \log \mu\mu$ , and the mean value of normals for the age group into which each individual miner fell. Thus a miner of 34 years of age who gave a result of  $2.11 \log \mu\mu$  was entered as having an adjusted value of  $2.24 \log \mu\mu$  in the 40/50 age group, since the mean value of normals (Table I) for the 40/50 age group ( $2.07 \log \mu\mu$ ) is  $0.13 \log \mu\mu$  higher than the mean value for normals in the 30/40 age group ( $1.94 \log \mu\mu$ ). The mean value shown for each group (a) to (e) is the average of the individually adjusted values.

### Observations

It will be seen that the threshold value in each group (a) to (e) is substantially higher than for the normal  $2.07 \log \mu\mu$ . This is particularly of interest in the case of group (e), miners who show no evidence of the disease, either in respect of eye movements or other symptoms. Practically all these men, however, were obtained for test by reason of their having been at one time or another Eye Hospital patients who had reported an account of minor eye injuries or defective sight.

No discussion of the significance of the results is being attempted here, as this is being dealt with by Dr. Dorothy Campbell elsewhere in this issue, in the light of a full series of other tests on the same men.

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# A COMPARISON OF DARK ADAPTATION IN MINERS WITH THEIR NUTRITIONAL STATE

BY

DOROTHY ADAMS CAMPBELL and EVA TONKS

FROM THE RESEARCH DEPARTMENT OF THE BIRMINGHAM EYE HOSPITAL

A CAREFUL inquiry was made into the nutritional state of about 100 miners—i.e., their access to food, choice of diet, number in family, etc. In addition, estimations of plasma vitamin A and of carotene were undertaken to run parallel with the dark adaptation tests, to ascertain whether they were commensurate with the threshold value. The possibility of a deficiency in vitamin D was also considered, since miners working underground sweat heavily and are likely to lose surface fat, i.e., potential vitamin D. Moreover, they are rarely exposed to sunlight which favours the manufacture of vitamin D, and the present day diet is unlikely to produce the required daily intake of 300-600 I.U. of vitamin D. The estimation of plasma alkaline phosphate was taken as the indication of any possible deficiency of vitamin D, while a liver function test was used as a check against the possibility that an abnormal vitamin A content, or a raised blood phosphatase might be due to liver dysfunction.

The normal range for the blood constituents is as follows:—

Plasma carotene	...	...	...	50-240 $\mu$ g per 100 ml.
Vitamin A	...	...	...	70-140 I.U. per 100 ml.
Alkaline phosphatase	...	...	...	5-10 units per cent.
Liver dysfunction test.	0.0	—	1.68 ml.	(by thymol turbidity method) barium sulphate suspension (average 0.63)

On analysis it was found that:—

(1) There was no parallelism between the threshold value and the level of vitamin A in the blood taken at the time of examination (either in surface or underground miners and in controls or in those with nystagmus). (See Tables I and II.)

(2) There was no significant variation in the plasma vitamin A or D in comparison with age, occupation, or incidence of nystagmus. The plasma vitamin A tends to be higher in non-miners and in miners working on the surface, than in those afflicted with nystagmus and in normal miners working underground (Table III).

(3) There was no evidence of any disturbance in liver function in the individuals tested (Table III).

(A) Owing to the system of rationing there was no seasonal variation in the dietary content of vitamin A, nor in the choice of diet available.

TABLE I

*Comparison of blood vitamin A level with threshold of dark adaptation surface workers*

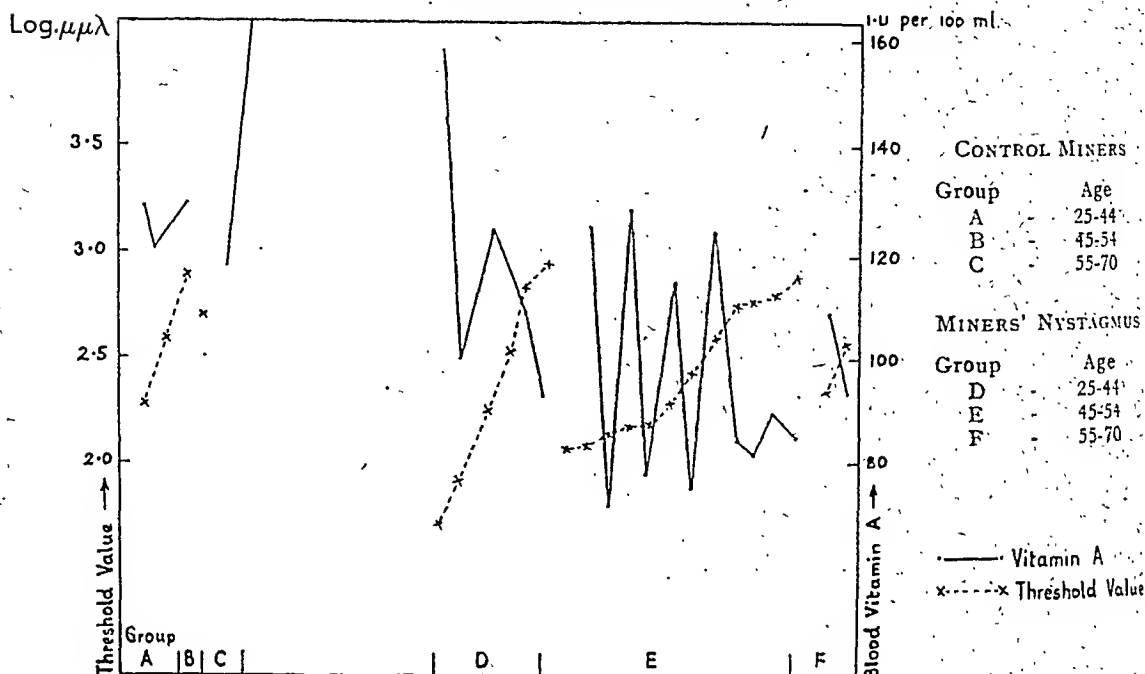


TABLE II

*Comparison of blood vitamin A level with threshold of dark adaptation underground workers*

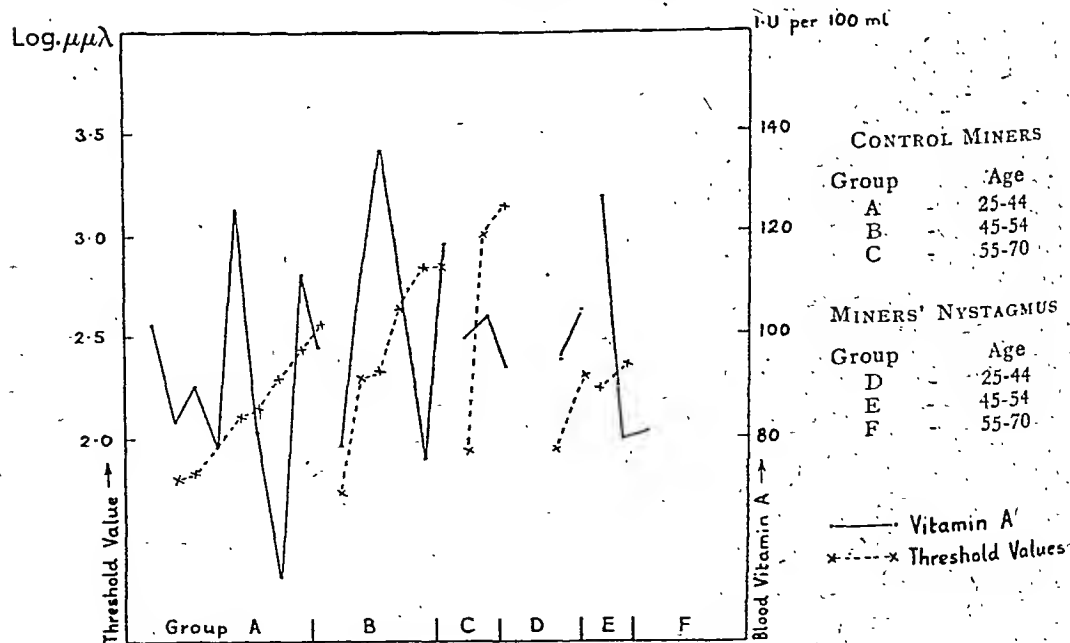


TABLE III. *Biochemical Investigations classified in  
types of worker*

*Miners' Nystagmus : Underground workers*

Age Group	Carotene $\mu\text{g } \%$	Vit. A. I.U. $\%$	Alk. Blood Phosphatase Units $\%$	Liver Function Test Thymol Turb. ml. BaSo <sub>4</sub> susp.	Threshold Dark Adaptation Log. $\mu\mu\lambda$
Under 25	—	—	—	—	—
25-44	36 (5)	90 (5)	8.1 (2)	0.40 (2)	2.14 (2)
45-54	92 (4)	94 (4)	6.3 (2)	0.29 (2)	2.59 (3)
55-70	110 (1)	82 (1)	—	—	2.21 (1)
All ages	65 (10)	91 (10)	7.2 (4)	0.35 (4)	2.38 (6)

*Miners' Nystagmus : Surface workers*

Under 25	—	—	—	—	—
25-44	79 (7)	118 (7)	7.3 (4)	0.27 (3)	2.37 (8)
45-54	66 (18)	94 (18)	8.5 (9)	0.37 (3)	2.39 (14)
55-70	69 (6)	93 (6)	9.0 (3)	—	2.44 (4)
All ages	70 (31)	99 (31)	8.3 (16)	0.32 (6)	2.39 (26)

*Control Miners : Underground workers*

Under 25	67 (4)	94 (4)	7.2 (2)	0.35 (2)	—
25-44	56 (19)	98 (19)	7.3 (11)	0.33 (10)	2.12 (9)
45-54	68 (13)	101 (13)	8.8 (6)	0.40 (5)	2.47 (6)
55-70	65 (8)	95 (8)	7.9 (4)	0.49 (4)	2.71 (3)
All ages	62 (44)	98 (44)	7.8 (23)	0.38 (21)	2.33 (18)

TABLE III—*continued**Control Miners: Surface workers*

Age Group	Carotene μg %	Vit. A. I.U. %	Alk. Blood Phosphatase Units %	Liver Function Test Thymol Turb. ml. BaSO <sub>4</sub> susp.	Threshold Dark Adaptation Log: μμλ
Under 25	—	—	—	—	—
25-44	112 (4)	115 (4)	9.5 (2)	0.4 (2)	2.41 (4)
45-54	60 (5)	89 (5)	7.3 (4)	0.5 (4)	2.34 (2)
55-70	68 (7)	108 (7)	6.7 (5)	0.39 (5)	1.92 (2)
All ages	77 (16)	104 (16)	7.4 (11)	0.44 (11)	2.27 (8)

*Normal Controls: Not miners*

Under 25	69 (2)	113 (2)	—	0.78 (1)	1.52 (43)*
25-44	72 (24)	111 (24)	6.4 (3)	0.46 (9)	1.95 (53)*
45-54	93 (4)	116 (4)	6.2 (1)	0.44 (3)	2.11 (24)*
55-70	61 (16)	97 (16)	8.8 (6)	0.59 (10)	2.18 (5)*
All ages	70 (46)	107 (46)	7.8 (10)	0.53 (23)	—

Note: Results are expressed as the average figure in each group.

Figures in brackets = number of cases.

\* Threshold values in this group not concurrent with biochemical investigations.

**Conclusion**

Although the evidence from biochemical tests is not dramatic it demonstrates clearly that the raised threshold for dark adaptation which is a constant feature among miners—including those suffering from nystagmus—is not due to a lack of vitamin A or D, or to any obvious nutritional disturbance.

## THE PSYCHIATRIC ASPECT OF MINERS' NYSTAGMUS.—I.

BY

EDWARD S. STERN

CENTRAL HOSPITAL, WARWICK

MINERS' nystagmus is the third most important cause of invaliding from the pits, coming after pneumoconiosis and the "beats" (limb injuries). But it is unlike them in having no morbid anatomy nor clinical pathology and in that the patient suffering from it presents no objective physical signs, though he is prolific in the production of protean subjective symptoms. This investigation was undertaken in order to estimate how far the disease was of emotional as opposed to physical origin.

It is not possible to assess the emotional factor in any case perfunctorily, and so statements that some patients either do or do not show psychoneurosis are valueless unless based on adequate psychiatric examination by a physician trained in psychological medicine. Indeed, such opinions by many doctors are inclined to be of less value than those of the man in the street, owing to the bias of medical training away from mental and towards physical pathology.

It is not claimed that emotional disorder was discovered in all cases in whom it existed in this series, for the psychiatric interview only lasted a half to three quarters of an hour, and further observation under residential conditions would have made the examination more complete, but it is hoped that adequate diagnosis and assessment were made in most patients.

### Method of examination

It was first explained to the patient that this investigation was proceeding and we were anxious to see if his nerves were affected or could be helped in any way.

He was then seated in a comfortable chair and after his name, address, etc., had been noted, he was asked of what he complained and its duration.

All his past physical illnesses, operations, and serious accidents were then carefully noted, as were any past mental or nervous disorders.

His father's occupation, and the age and state of health or cause of death of each parent, with the patient's age at the time, together with particulars of the siblings, and the patient's position in the



family, were obtained. Particulars were also obtained as to his own children and their state of health.

He was asked whether he had been happy as a child, whether the home was happy, and his emotional relationships to each parent. Also, whether he liked school and the standard attained, with any further education.

Particulars were obtained of all his past employments and the time he spent in each post. He was asked whether he liked mining.

Enquiry was then made into the patient's relationship to his wife, and in most cases into his sexual life. He was asked if his house and home were satisfactory.

His economic circumstances, amusements, religion, sleep, dreams, alcohol and tobacco consumption, appetite, and excretion were enquired into.

An effort was made to find if he showed obsessional traits. His appearance, behaviour, cleanliness, and dress were next noted.

At this stage his ophthalmic out-patient sheet was read for the first time, and his eye movements were examined for the presence or absence of nystagmus, etc.

Enquiry was then made into any further circumstances that appeared significant, and a psychiatric diagnosis was made.

Subsequently the psychiatric case sheet was perused and summarised.

## Psychiatric summaries of individual cases

### (a) *Certified cases with active nystagmus*

E.B.—A dull and backward man who has developed hysteria and considers that the colliery has treated him shabbily. He now complains of giddiness and visual symptoms. Diagnosis: dull and backward person, hysteria, rotatory nystagmus.

E.W.B.—An extremely indolent man who has stopped work following an accident. His nystagmus of lateral type appeared to me to be voluntary and the result of conscious effort. He complains of giddiness and visual symptoms, but I doubt whether his disorder can be dignified by the name of hysteria—"I'd like a light job in the colliery."

When asked what his principal amusement was, he said, "Nothing much, I just sit in a chair." In looking for obsessional acts, I asked him if he ever had to go down from his bed to see if he had left the gas on, and he replied, "No. If the gas is left on I don't go down, the wife has to." This sufficiently sums up his character. Diagnosis: traumatic neurasthenia (compensation case).

T.D.—Anxiety neurosis with conversion hysteria.

J.T.D.—This man suffers from severe anxiety, which he tries to deny. His apprehension was patent to all, but he said, "No, I was not nervous waiting to see you." However, as soon as I let him go he rushed away as if very frightened. Diagnosis: anxiety neurosis, with hysterical conversion symptoms.

W.H.—This man is of the "fire-eater" type, with an Oedipus complex. He complains of quadruple or quintuple shifting vision, which has only come on since he was diagnosed as suffering from nystagmus. He complains that he cannot boss or be bossed, and is proud of having suffered numerous accidents. Although his anxiety is partly converted into hysteria, fixated on his eyes, on examination the

rotatory nystagmus in his left eye appeared quite genuine, as if he was peering or groping to see, reminding one of Milton's famous lines:

"These eyes, that rowle in vain

To find thy piercing ray, and find no dawn."

"Paradise Lost," III, 11/23-24.

It may be that the anxiety was secondary to the nystagmus. Diagnosis: anxiety state, with conversion and fixation hysteria.

J.H.O.—A manic-depressive now, as usual, in a melancholic phase, apprehensive of his eyes, but whose visual symptoms are subjective. He is dull and backward, childish, and dependent. Diagnosis: melancholia, dull and backward.

J.T.W.P.—A mildly schizoid personality. Diagnosis: dull and backward.

C.J.P.—A solitary type, suffering from hysteria with diplopia and other visual symptoms; he never liked mining, entered the industry reluctantly, and readily left it. Diagnosis: hysteria.

G.N.P.—This man has an obsessional character and it is probable that his anxiety is mainly a result of his nystagmus. He has numerous hysterical conversion symptoms. Diagnosis: anxiety neurosis, with conversion hysteria.

A.E.R.—Conversion hysteria in a sensitive man suffering from anxiety and severe feelings of inferiority, with masturbatory guilt. Diagnosis: anxiety neurosis, with hysterical conversion symptoms.

F.R.—Diagnosis: hysteria.

J.W.S.—This man is so dull and demented that it is difficult to make any further diagnosis, but he is probably hysterical. Diagnosis: dementia.

H.S.—Rather a dull man. Diagnosis: anxiety neurosis, with conversion hysteria.

F.F.S.—Diagnosis: mild anxiety state.

D.W.—An over-conscientious man, and an obsessional type, who has finally broken down with frank anxiety. In addition, his wife is hallucinated and on one occasion had to enter a mental hospital owing to dementia praecox.

### (b) *Certified cases showing no nystagmus*

W.A.—The above is a hysteric whose symptoms are so severe that he is almost psychotic.

A.H.B.—Diagnosis: dull and backward. Mildly manic-depressive, probably hysterical.

R.W.C.B.—A dull man, who was always an unwilling pit worker, apprehensive of accidents, and developed an anxiety neurosis with hysterical conversion symptoms. He is suspicious and has some sexual guilt of which he is ashamed. Diagnosis: anxiety neurosis, with hysterical conversion symptoms, in a dull and backward subject.

S.B.—This man appears work-shy and was apprehensive in the pit—"I used to dread it and fear that the roof would fall down on me, I fear I have had enough pit work."

He is now working as a blacksmith's assistant and says of this post, "I like the work very much now, I could not have picked a better job—there are days when I don't do a tap." He is dull and backward.

The most charitable diagnosis is one of hysteria, though I cannot help doubting whether his symptoms are below the conscious level, or he is malingering.

B.D.—When I examined this man's eye movements he deliberately thrust his head back and looked upwards, and there was some slight left lateral nystagmus, which seemed to me to be voluntary. It is charitable to consider him a hysteric. Diagnosis: hysteria (or malingering).

S.D.—This man's attention was first drawn to his trouble by his doctor and then by his daughter. The few symptoms had not worried him previously. "Before that, on my pay ticket the figures were too many without my glasses on, i.e., I saw double." His case began with diplopia. He now presents no mental symptoms or signs, but has a few subjective complaints. However, he protests that he would like to be down the mine—"I would rather be there than on the bank—do you know, you simply can't be sure of the weather above ground!" Diagnosis: normal (or malingering).

R.E.—This man has had various subjective symptoms, which were possibly hysterical, but he now has no complaints. Diagnosis: normal.

E.F.—An over-conscientious, obsessional man, who shows anxiety when he thinks he fails to reach his own excessively high standards. Diagnosis: conversion hysteria resulting from an anxiety state in an obsessional man.

H.F.—An immature, emotional, unstable subject, with an anxiety neurosis and some hysterical conversion symptoms. His complaint of feeling disinclined to work on some days is probably unrelated to his eyes, but he was told by a doctor that he had "eyestagmus." He subsequently had an accident to his back, since when he has not been down the pit, but being unable to live on the money he received he took on his deceased uncle's chimney sweeping business, which he does when he feels so inclined. He is still childish and dependent and weeps when he tells how well he gets on with his Dad. Diagnosis: hysteria.

E.Hu.—When I made to examine his eyes, his blepharospasm and twitching of the lids increased before I even asked him to fix his vision. At the same time he twitched the right side of his face and the corner of his mouth. His eye movements were normal, but he showed voluntary convergence from time to time as he fixated a near object, though there was no nystagmus. Diagnosis: hysteria.

E.M.—This man describes hallucinations and is fundamentally psychotic. He is also apprehensive in the pit owing to an anxiety neurosis with some conversion symptoms partly fixated on the eyes. Diagnosis: anxiety neurosis with conversion hysteria in a schizophrenic.

J.Mc.—This man is deaf. Diagnosis: hysteria.

J.M.P.—His only complaint was of the consequences of an injury to the right malar region, and he said that bending made his face swell up on that side, and so he could not again stand going down into the pit. He is a dependent type. Diagnosis: anxiety neurosis, dull and backward.

E.R.—This man has a bluff Falstaffian manner which conceals deep anxieties, and he shows hysterical conversion symptoms. He is rather exalted, as his son is a high union official, and is resentful of his treatment by the colliery, being strongly interested in his compensation. When I asked him whether he preferred candles, Davy lamps, or electric lighting, he replied, "I like candles best, you can tell when your shift is nearly up by the number of candles you've burnt." He has some anxiety and it is kindest to describe him as a "hysteric." Diagnosis: hysteria (or malingering).

J.H.R.—A man with much fear of mining. Diagnosis: conversion hysteria with some anxiety.

A.Sma.—A truculent man, who may well once have been attentive to his work, but has, not unnaturally, given it up in his old age. He is very interested in compensation. Diagnosis: hysteria.

T.G.S.—A rather dull man who has various anxieties, e.g., a fear of accidents in the pit, of which he is ashamed, which he tries to hide. Diagnosis: anxiety, with conversion hysteria.

F.H.S.—Diagnosis: anxiety, with fixation and conversion hysteria.

H.Ta.—This man has a rigid, closed mind. He wears dark glasses, which seem to symbolise his wish not to see things clearly, and is sensitive and suspicious. He said, quite gratuitously, "I told the step-son that if he gets into trouble he must go to someone else for help, as he will get none from me." The patient's own anxieties may well be derived from his unsatisfactory marital life. Diagnosis: anxiety neurosis, with conversion hysteria.

R.T.—Diagnosis: hysteria.

T.T.—This man has no complaints. Diagnosis: N.A.D.

H.W.—An evasive and suspicious man, who feels he has had a poor deal from life. He is apprehensive, fearing he may lose his compensation. Diagnosis: melancholia.

A.W.—Diagnosis: hysteria.

W.B.W.—A recurrent melancholic, of poor intellect, now showing some dementia. It is possible that he previously suffered from a psychoneurosis. The first attack of melancholia occurred when his wife died  $5\frac{1}{2}$  years ago. Diagnosis: melancholia, with secondary dementia.

(c) *Early, no nystagmus*

C.H.—Possibly there is incipient nystagmus in a high myope. Diagnosis: normal.

G.W.L.—An obsessional neurotic, who develops anxiety in certain situations and has some hysterical conversion symptoms and a well marked Oedipus complex. Diagnosis: obsessional neurosis, with anxiety and conversion symptoms.

A.R.—A mild manic-depressive, now in a melancholic phase, with some sexual guilt. Diagnosis: melancholia.

H.Tw.—An able, over-conscientious obsessional, of the type who drives himself and others, and is usually found in a position of minor authority, this man being a colliery deputy. His anxieties arise when he is unable to satisfy his compulsive demands. Diagnosis: obsessional neurosis, with some anxiety.

G.H.W.—A dull and backward man, capable of doing a simple task slowly, but showing anxiety when harassed. Diagnosis: high grade mental deficiency, with anxiety and conversion hysteria.

(d) *Active nystagmus. No symptoms. Working*

W.G.A.—He is now in a mild melancholic phase. Diagnosis: mild manic-depressive.

E.S.G.—A dull and backward man, with no other mental symptoms.

W.H.M.—This man showed me that he can bring on or stop a left lateral nystagmus at will. He is mildly obsessional. Diagnosis: normal.

(e) *Controls, no nystagmus*

F.J.J.A.—A conscientious and easily worried man. Diagnosis: mild obsessional neurosis.

R.B.—A mildly obsessional personality. Diagnosis: normal.

E.A.B.—Now a little melancholic. Diagnosis: manic-depressive.

H.H.B.—This man's depression may have followed his wife's death. Diagnosis: mild chronic melancholia.

J.B.B.—Diagnosis: normal.

T.C.—Intelligence poor. Possibly some hysterical conversion symptoms. Diagnosis: either dull and backward or a little demented, anxiety neurosis.

J.W.C.—Now a mild chronic melancholic. Diagnosis: chronic melancholia, with exacerbations.

J.R.D.—This man has hysterical conversion symptoms referred to his stomach. Diagnosis: anxiety neurosis.

W.J.G.—He is depressed and hypochondriacal. Diagnosis: mild manic-depressive.

J.H.—Diagnosis: normal.

E.H.—He is suffering from an exacerbation of anxiety caused by a fractured base of skull. Diagnosis: mild anxiety state.

J.W.H.—He has domestic trouble, his wife having left him. Diagnosis: normal.

H.J.—Diagnosis: normal.

C.K.J.—This patient is seriously psychotic and feels suicidal. I advise his immediate admission to an institution. Diagnosis: recurrent melancholia.

A.B.K.—A dull, anxious man, lacking confidence and drive. He has an early cataract, with fixation hysteria, giving him giddiness. Diagnosis: anxiety neurosis, with hysterical conversion symptoms, in a dull subject.

H.M.—Occupation: underground bricklayer. Superficially he at once seemed to be a different type from the miners. He is rather dull and investigation revealed his psychoneurosis. Diagnosis: obsessional neurosis.

J.M.—This man has some latent anxiety with early conversion symptoms, and it is possible that he has incipient miners' nystagmus. Diagnosis: normal.

E.T.R.—Diagnosis: anxiety neurosis, dull and backward.

W.S.—This man is mildly obsessional, but within normal limits. Diagnosis: dull and backward.

A.Smi.—Diagnosis: chronic melancholia (mild).

J.H.T.—A typical cockney—a different type from the other miners. Diagnosis: normal.

D.T.—He was not interested in the investigation and so his answers were careless and possibly inaccurate. Diagnosis: normal.

J.L.W.—A mildly obsessional personality. Diagnosis: normal.

### Tabulated Summary

Groups	Normal	Malingering	Hysteria	Anxiety Neurosis	Obsessional -Neurosis	Dull and Backward	Manic- Depression
(a) Certified Cases with Active Nystagmus ...	—	—	6	6	—	2	1
(b) Certified Cases showing no Nystagmus ...	2	3	9	7	—	1	2
(c) Early, no Nystagmus ...	1	—	1	—	2	—	1
(d) Active Nystagmus. Nosymptoms. Working. ...	1	—	—	—	—	1	1
(e) Controls (no nystagmus) ...	8	—	—	5	1	2	7

### Classification

The cases in this investigation are given above under the classifications made by the ophthalmologists, *viz.*:

(a) Certified cases of miners' nystagmus with oscillations.

(b) Certified cases of miners' nystagmus showing no oscillations.

(c) Suspected early cases, not showing oscillations.

(d) Cases showing ocular oscillations, but working, without symptoms.

(e) Controls.

It must be remembered that not all those classified as miners' nystagmus show, or indeed ever have shown, any rotatory or other oscillations of the eyes, and that possibly a few labelled normal or hysterical may have been malingerers. With these reservations, the nystagmus cases mostly show hysterical conversion symptoms, though in some cases, as indicated, the basic diagnosis is otherwise, *e.g.* mental defect or melancholia, the former being notoriously prone to hysteria and the latter showing nystagmus symptoms as a somatic aspect of their malady. As

would be expected, the symptoms represent a conversion of anxiety and where this is incomplete the basic diagnosis is one of anxiety neurosis rather than hysteria, but the two are complementary and not mutually exclusive. The small number of obsessionals were over-conscientious men whose failure to reach their own high standards resulted in anxiety, some of which was converted into hysterical symptoms.

There is good reason to believe that possibly the photophobia, subjective rotation of objects, giddiness, blepharospasm, and headaches, are hysterical in nature and of emotional and not organic origin.

### Symptoms

Of the patients certified as suffering from miners' nystagmus, the 15 classified as showing active rotatory nystagmus and the 24 not showing this sign complained of the following leading symptoms, with the respective frequencies shown in parentheses.

Visual symptoms which could be referred to an organic lesion in the eyes:—

(0, 1).

Visual symptoms which could not be so referred:—

Blindness (1, 2).

Difficulty in seeing or inability to focus (2, 0).

Dazzle (2, 3).

Double or multiple vision (2, 0).

Subjective rotation or movements of objects (2, 8).

Shakiness of the eyes (1, 0).

They also complained of the following, which are ordinary psychoneurotic symptoms not usually related to disease of the eyes:—

Stiff neck (1, 0).

General shakiness (1, 0).

Giddiness or drunken feelings (8, 11).

Headaches (2, 10).

Insomnia and dreams (0, 2).

Noises in the head (1, 0).

Nervousness and anxiety (1, 2).

Depression (1, 0).

Loss of interest in reading and writing (0, 1).

Disinclination to work (0, 1).

In addition, 3 of the second group complained of pain in the eyes, and 2 stated that they now had no symptoms at all.

The 23 controls complained of 19 leading symptoms such as

would be expected from their physical condition (two being of diplopia) and also of dazzle (3), subjective rotation or movements of objects (1), giddiness (2), headache (1), fear of blindness (1).

The difference between the first two of these groups and the third is striking, and strongly suggests that the former have little objective eye disease but are suffering from psychoneurosis, in contradistinction from the latter, who were a series of ordinary ophthalmic miner out-patients. This is confirmed by calculation which shows the correlation between psychoneurotic symptoms and the first two groups to be positive and statistically significant ( $Q$ =coefficient of correlation = +0.8).

The three cases with asymptomatic rotatory nystagmus made no complaint not referable to organic disease of the eyes, for two had corneal ulcers and one had presbyopia. The five cases of suspected early miners' nystagmus complained of no symptoms which could be referred to organic eye conditions, but of apparent oscillation of objects (1), giddiness (1), headache (3). But these last two groups are too small for any firm conclusion to be drawn from them.

#### Predisposition to mental illness and miners' nystagmus

Of the 15 patients certified as suffering from active miners' nystagmus and showing active rotatory movements, and the 24 certified cases without this sign, 4 (27 per cent.) and 9 (38 per cent.) respectively gave a history of unsatisfactory emotional conditions in infancy, while 5 (22 per cent.) of the 23 controls did so. The differences between those affected and the controls do not appear significant, and so it is improbable that this is a major aetiological factor in the disease. It leads one to suspect that breakdown in the first two groups did not readily occur, but only after unusually severe or prolonged emotional stress in the mines.

A history of previous mental instability was given by 1 (7 per cent.) and 7 (28 per cent.) respectively of the first two groups, against 6 (26 per cent.) of the controls, and the same arguments apply.

It was found below that miners' nystagmus only occurred after many years' work in the mines, which accords with the above.

It was found that the certified cases did not give a history of a significantly greater number of minor ailments or accidents than the controls, suggesting that up to the onset of symptoms their service had been satisfactory as regards absence for health reasons. It must, however, be admitted that only a perusal of their work records can confirm this.

The above facts indicate that it is unlikely that future cases of

miners' nystagmus could be eliminated by any method of selection on entering the industry, and that even if this were possible, it would be unwise to exclude from the mines a body of men who would give many years of satisfactory service before breakdown.

### Statistical considerations

The social and similar data were carefully compared in the three major groups. The findings in the two smaller groups were also considered but their numbers were insufficient for analysis.

At the onset of symptoms the ages of the certified cases of active rotatory nystagmus showed a range from 29–71 years, with a median of 43 and a probable error of 4.0. The corresponding ages of the certified cases not showing this sign showed a range of 29–71 years with a median of 45 years and a p.e. of 3.5. The differences between the means in the first two groups (43 and 45.7) were found not to be statistically significant, and since the curves were of similar form they have been combined in a histogram in Fig. 1. The controls had a corresponding age range of 0 (the next figure being 24)–61 years. The graph shows that we

FIG. 1. Ages shown in quinquennial periods, at onset of symptoms

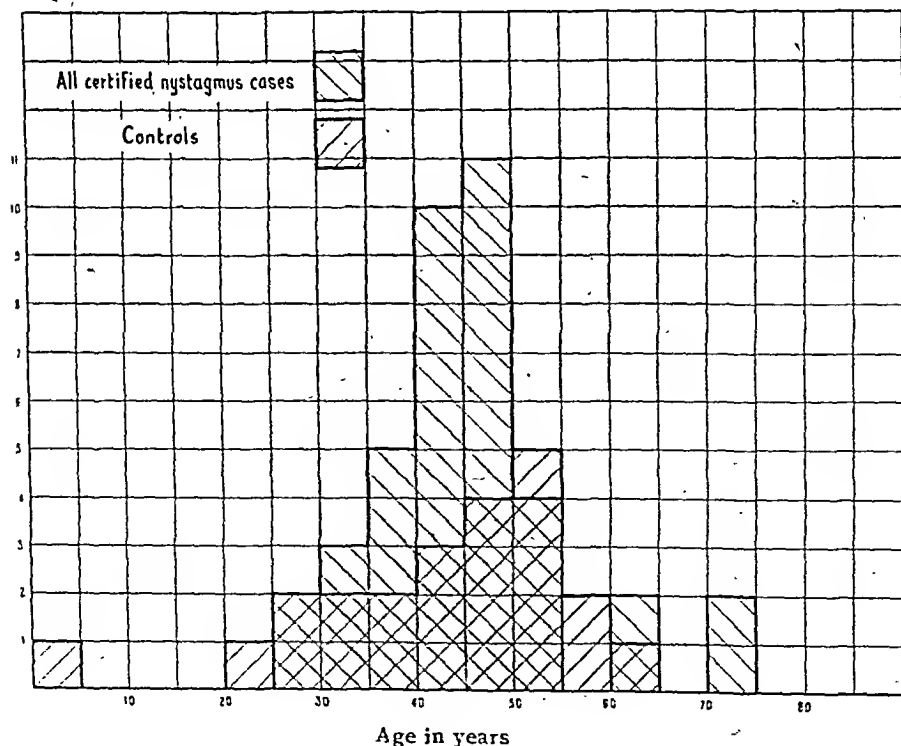
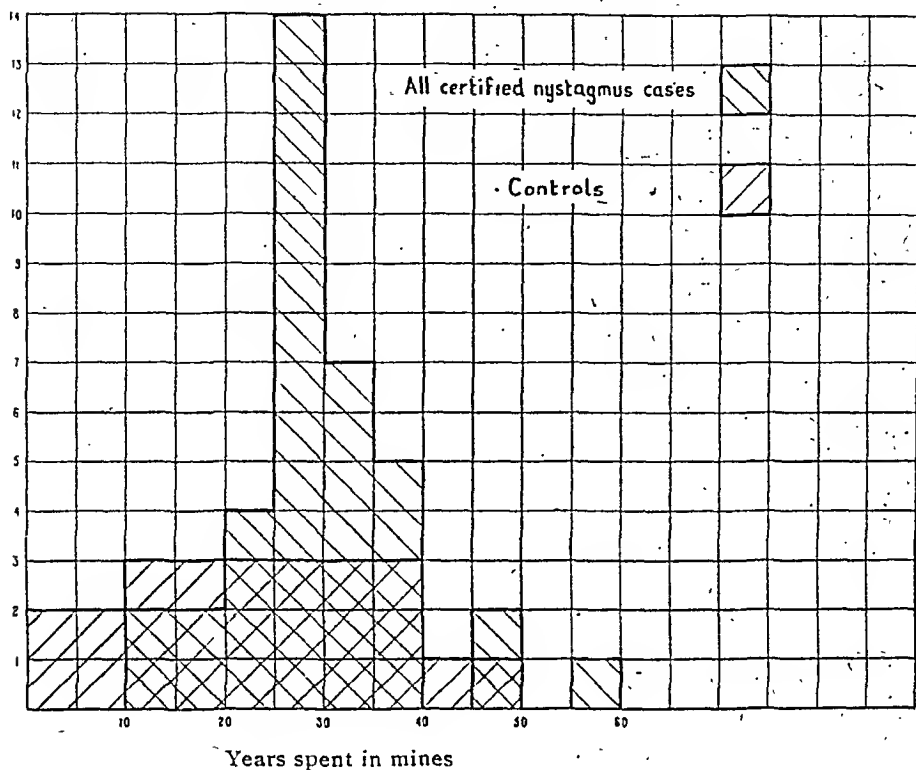




FIG. 2. Years, shown in quinquennial periods, spent in the mines before the onset of symptoms



are not here dealing with a curve of normal frequency but more probably with an average sample of the mining population, which contains a slightly younger (mean 41.5) body of men. This means that the controls are not truly comparable with the affected cases, but it also demonstrates that they form a group distinct from the first two, each of which gives a similar type of curve. Eight of the 15 in the first group and 13 of the 24 in the second, but only 7 of the 23 controls fell within the age group 40—49 years.

At the onset of symptoms, the 13 certified cases of active rotatory nystagmus from whom such data were obtained, had worked a range of 11—59 years in the mines, with a median of 30 years and a p.e. of 5.0; the 24 certified cases without this sign had worked a range of 11—47 years in the mines, with a median of 27 years and a p.e. of 3.0. The difference of the mean (29.1 and 28.7) in the two groups were found not to be statistically significant and so, as the curves were of similar shapes, they have been combined in the histogram of Figure 2. The 23 controls had worked a range of 0—46 years in the mines, with a median of

24 years and a p.e. of 10.5 (mean 23). Once again the controls do not show a curve of normal frequency and the same considerations apply as in the last paragraph. Six of the 13 in the first group had worked 25—34 years in the mines at the onset of symptoms, as had 15 of the 24 in the second group, against 6 of the 23 controls. This corresponds with the findings as regards age, since most of the men enter mining when 14 or 15 years old—See also Graph V, First Report (1922, p. 51).

### Social findings

The 15 certified cases with active rotatory nystagmus and the 24 certified without this sign have an average of 9.3 and 8.2 siblings respectively, of whom 1.5 and 2.1 have died, so that 7.8 and 6.1 survive; the corresponding figures for the 23 controls being 5.8 born, 1.1 dead, and 4.7 surviving. This suggests that the latter had known less privation and a healthier family life in childhood. (The corresponding figures for numbers of children in the three groups are: 3.3, 3.2, 2.6 born, with 0.2, 0.5, and 0.3 dying, leaving 3.1, 2.7, and 2.3 surviving, the numbers in the control series being the smallest, possibly because of the lower ages of the fathers. This matter, though not germane to our present investigation, must give rise to apprehension about the future labour force in a largely hereditary industry.) The father of the patient was a miner in 13 out of the 15 and 17 out of the 24 of the first two groups, against 14 out of the 23 controls; so that such parentage is not a favourable one as regards liability to this disease ( $Q = +0.3$ ).

The number of collieries in which the miners in each group worked was not significant, but the first two groups of 15 and 24 miners had on 4 and 12 occasions respectively to leave the mine presumably at the usual fortnight's notice owing to its closing, but in the 23 controls this had only happened twice. Even having regard to the total average number of years spent in the mines, 32 in each of the first two groups against 26 in the controls, these numbers seem significant ( $Q = +0.6$  and  $+0.9$  respectively) and suggest that insecurity of employment is an aetiological factor in miners' nystagmus.

### Mechanism of rotatory nystagmus

The oscillations of the eyes are generally striking, unique, rapid, and circular or elliptical.

Lateral nystagmus is sometimes seen in hysterics and a few subjects can produce it voluntarily by strong convergent fixation.

When a person enters the dark he converges strongly and it may well be that lateral nystagmus can be thus produced. In this connection it is interesting that it has been reported that, during the war, night fliers, who were subject to considerable emotional strain, sometimes complained of subjective lateral oscillations of the tail light of the aeroplane in front as an early symptom in mental breakdown. Besides working in the dark, the miner is often in an awkward and stooping attitude when walking and when having to hew coal above his line of vision, so that he is obliged to look upwards, the relative positions of his eyes and body being contrary to the static reflexes of Magnus and de Kleijn. An upward gaze is always difficult to maintain, and so we should expect that, owing to rapid fatigue, the eyes would continually tend to turn downwards and repeatedly have to be brought back upwards—with the production of a vertical nystagmus.

Now the directions of the horizontal and vertical excursions are at right angles. Each nystagmus is a periodic movement and so can be resolved into one or more simple harmonic motions and should be regarded as consisting of these components. We have then the case of s.h.m.'s at right angles, if they are of the same frequency their sum will be a circular or elliptical movement, unless one component is negligible when it will be lateral or vertical, and except in the rare instance where they are in the same phase, when it will be diagonal, as has been noted (First Report, 1922, p. 20). Thus it appears that the rotatory oscillations of miners' nystagmus are the summation of a vertical and a horizontal nystagmus resulting from darkness and prolonged upward gazing.

If these mechanisms are taking place in the higher centres of the brain, the precise muscles involved are immaterial, since these centres deal with integrated movements only and not with individual muscles. These nystagmoid movements will only develop in the conditions named, *viz.*, darkness and sustained upward gazing in the normal subject, but in the hysteric, once they have been learned, there is the possibility of their occurrence in the light and when looking in a normal direction, though they will still be particularly easily elicited by darkness, strong convergence, or upward gazing, which is what is found in miners' nystagmus.

### Discussion

Amongst the various suggested causes of miners' nystagmus are focal sepsis, in the days when such a belief was popular (O'Sullivan, 1932), increase of blood pressure on entering the pits (Idem, 1936), failure of dark adaptation owing to lack of Vitamin A (Campbell, 1941), and even spontaneous combustion (Sack,

1925). But these have failed to pass the tests of experience or investigation. The work of Roche (1932), Zeiss (1932), and the First and Third Reports (1922 and 1932), indicate darkness as an aetiological factor. This darkness is more profound in "safety light," and therefore dangerous, pits, where a greater stress due to fear is present. It was early believed that awkward posture was an important cause (First Report, 1922), and as long ago as 1725, the Manchester Justices fixed a rate of 1s. 3d. a ton for Lancashire colliers getting coal in a high delf, and only 1s. a ton in a low delf (Rogers, 1891). Elworthy (1925) showed that the incidence of miners' nystagmus varies inversely with regular work and high wages, and Collis (1925) attributes it to economic anxiety. Dickson (1933) pointed out its similarity to shell-shock. Brock (1938) considers it psychoneurotic, Butler (1939) calls it "miners' neurosis."

In their investigation of telegraphists' cramp, Smith, Culpin, and Farmer (1927) state: "It is pertinent to enquire why telegraphy should have a specific 'cramp,' when other occupations of an allied nature have not . . . the exacting nature of the work, the inevitable rigidity of the conditions, the isolation of this one symptom, with its disabling effects, have all operated to concentrate attention into this channel. . . . In England telegraphy is a permanent occupation . . . in America there is more mobility of labour and the disease is hardly recognised . . . Should such general conditions become characteristic of any other allied occupation, we should expect a similar result, *viz.*, some form of disability affecting that part of the body which is most used or essential for the particular process, and the people likely to be affected to be . . . the psychoneurotic. Expressed more generally, a person emotionally unstable working in an environment either actually, or conceived by him as, inflexible will have just that interaction of conditions necessary for 'cramp' or some similarly determined disorder." In the Third Report (1932, p. 16) Culpin showed miners' nystagmus to be a psychoneurosis.

From the above and the investigations in this paper, it is evident that miners' nystagmus is a disease of emotional origin, commonly called hysterical, hysteria (Medical Research Council, 1941) being "a condition in which mental and physical symptoms not of organic origin are produced and, maintained by motives never fully conscious, directed at some real or fancied gain to be derived from such symptoms," or a psychosomatic affection (Halliday, 1945), with eye symptoms, and is related to prolonged work under emotional stress in an awkward posture in the dark.

Now, in general, the characteristic of hysteria is that the

symptom can be imitated by a normal person. In miners' nystagmus this is not so, and the explanation is that the mechanism of the movements, as shown above, is so complex that it can only be learned, albeit unconsciously, by prolonged periods and emotional stress in an awkward posture in the darkness. It is thus a typical "occupational neurosis." In a case where the physical mechanism is so complex it is to be expected that the mental mechanism will also be complex, and so will not easily yield to treatment.

That some miners show the ocular oscillations without complaining of any symptoms, is not inconsistent with a diagnosis of hysteria. For which of us, when keeping an unwelcome appointment, or carrying out a distasteful task, has not heroically done his duty in spite of a headache, stiff neck, nausea, coryza, or even a "bone in the leg," which we bore with ascetic fortitude but without complaint; though this does not mean that if the emotional strain continued we should not eventually be disabled by our malady.

The true nature of the malady being established, it is evident that the presence or absence of the typical oscillations is relatively unimportant, merely representing a further stage in hysterical conversion of symptoms, and this is confirmed by the statistical similarity of the groups of miners' nystagmus with and without symptoms. Hence the alteration of the definition of 1906, "Miners' nystagmus is an occupational disease of the nervous system which is confined to workers in coal mines, and in ironstone mines where on account of the presence of thin coal seams safety lamps are used. The chief symptom and physical sign is a rotatory oscillation of the eye balls," to that of July 30, 1913, "The disease known as Miners' Nystagmus, whether occurring in miners or others, and whether the symptom of oscillation of the eyeballs is present or not"—would have been wise if only the malady had been recognised as of emotional origin and not in any way organic, and had been frankly called "Miners' Psychoneurosis."

If once the fact that the malady is psychological and not organic becomes generally recognised it is probable that the gross hysterical symptoms will become rarer and be substituted by frank anxiety, which is more amenable to treatment.

Mining is a dangerous occupation which subjects the collier to prolonged emotional stress, and so it is to be expected that the incidence of mental disorder of a mild type would be common in many such workers. This has been shown to be so in the series here investigated, not only in those certified as suffering from miners' nystagmus, but also in the 23 controls, and in accordance with the above we find (Table, p.214) that little behind the biggest group of eight normal men come the seven mild manic-depressives,

or cyclothymes, this being the adult reaction to prolonged and severe mental stress (Stern, 1944), whilst anxiety state is the next most common reaction. Conditions should be improved to lessen the emotional strain on the collier.

Miners have always tended to be a peculiar people. In Devon and Cornwall the tin miners had their own Courts of the Stannaries in the Middle Ages, the privileges of which were confirmed by Edward I as early as 1305, and were only abolished on the 1st January, 1897. The miner, too, is singular in that his occupation involves the spoiling, despoiling, disfiguring, and laying waste of his environment (Myres, 1946), his whole village lives on the destructive exploitation of the surrounding district, and when its mineral wealth is exhausted the community comes to an end; an end often sudden, unexpected, and catastrophic. His position is thus difficult and precarious. Miners are often vaguely conscious of these facts, and regard themselves, sometimes with reason, as a neglected and rejected people, their relation to the community being analogous to that of the neglected child to the parent, so that their behaviour often seems correspondingly irrational and irritating to their fellows.

Among themselves, however, miners form a closely-knit community, and this is especially so within the depths of the pits, for here is team work *par excellence*, and one weak, incompetent, or otherwise unsatisfactory member is a source of irritation, frustration, inefficiency, and lowered output, or even of positive danger to his fellows. It follows that if a miner has once had a severe emotional breakdown it must be doubted if he will again be readily acceptable to his workmates, for the true nature of such breakdown is often intuitively realised by them. This is yet another factor which may partly explain the common failure of nystagmus cases to remain for long in the pits when once they have been certified as suffering from this malady.

### Summary

1. Miners' nystagmus is a psychosomatic affection.
2. It arises from emotional stress, but for the full development of the oscillations a prolonged period of work in the dark with an upward gaze is also necessary.
3. The central mechanism of the oscillations is elucidated.
4. The emotional stress gives rise to anxiety and there is a varying degree of conversion of this into hysterical symptoms, which include the typical rotatory nystagmus, the presence or absence of which is relatively unimportant.
5. It does not usually develop until the miner has been underground for over ten years, more commonly for 25—34 years, and

although related to the stress and danger of the occupation it is unlikely that any psychological selection procedure could be devised to eliminate those likely to break down with nystagmus, before they enter the mines.

### Recommendations

1. The term "miners' nystagmus" should no longer be used, but all patients complaining of symptoms which would formerly have been considered under that heading should be referred to a psychiatrist as early as possible, for appropriate diagnosis and treatment, and should be certified as suffering from the actual psychoneurosis or psychosis found.
2. All such cases should be found work above ground and in the light, instead of being put on compensation. This work should be found as soon as possible, though a short period of rehabilitation may be necessary for psychiatric reasons.
3. They should be under psychiatric supervision.
4. Lighting in the mines should be improved.
5. Efforts should be made to ease the posture of the miner at work.
6. Special attention should be paid to safety measures in the mines.
7. The miner should be given economic security at his work.
8. Optimum hours of work in the mines should be worked out scientifically, and this matter should be removed from the sphere of politics.

I thank my friend, Dr. Dorothy Campbell for her kindness in inviting me to join in this investigation, for providing me with the necessary facilities, and for her constant encouragement and help, without which its completion would not have been possible, though it must be realised that the responsibility for the opinions expressed in this paper is mine alone.

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A COMPARISON OF DARK ADAPTATION WITH  
THE PSYCHOLOGICAL STATE IN MINERS

BY

DOROTHY ADAMS CAMPBELL

COVENTRY

LIVINGSTON and Bolton (1943) showed that the night visual capacity of different individuals might be due to varying attitudes of mind. Among 50 psychological in-patients of the R.A.F. those with an anxiety state were found to be incapable of concentration and to have a poor night visual capacity. Hysterics failed

TABLE I.—*Comparison with psychological state (65 cases).*

	Normal	Malingerer	Hysteria	Anxiety Neurosis	Obsess. Neurosis	Dull and Backward	Manic-Depressive
Early symptoms : no nystagmus	1'85 $\mu\mu\lambda$	—	2'49	—	1'83	—	2'11
Control miners with no nystagmus	3'01 2'85 1'83 1'77 2'67 2'31 1'85	— — — — — — —	— — — — — — —	2'85 2'01 2'59 2'01 3'17 — —	2'57 — — — — — —	2'37 2'67 — — — — —	2'89 2'17 1'95 2'35 2'13 2'31 1'81
Average	2'61 (7)	—	—	2'47 (5)	—	2'57 (2)	2'27 (7)
Certified cases with active nystagmus	— — — — — —	— — — — — —	2'35 2'27 1'91 2'81 1'97 2'07	2'25 2'07 2'25 2'17 2'31 2'75	— — — — — —	N.T. 2'57 — — — —	2'15 — — — — —
Average	—	—	2'23 (6)	2'29 (6)	—	2'57	2'15
Certified cases with no nystagmus	2'11 2'07 — — — — — — —	2'31 — — — — — — — —	2'59 2'93 2'13 2'37 1'71 3'1 * 2'47 —	2'33 2'41 2'21 4'21 * 2'51 2'89 2'47 2'79	— — — — — — — — —	2'8 * — — — — — — — —	3'16 N.T. — — — — — — —
Average	2'09 (2)	2'31	2'36 (6)	2'54 (7)	—	—	3'16
Active nystagmus with no symptoms	2'65	—	—	—	—	2'91	2'21
Average for all miners (65)	2'30(10)	2'31 (1)	2'30(12)	2'35(18)	(1)	2'68 (4)	2'45(10)

Figures in brackets = number of individual tests.

\* Tests done but not accepted as reliable.



markedly; whereas depressives even where some anxiety background had been revealed, seemed capable of making a reasonable effort.

Although the tests for dark adaptation do not involve the same mental judgment as night vision tests—it was considered interesting in the case of miners to compare the threshold values obtained by Dr. Sharpley with the psychological tests made by Dr. Stern. The results are recorded in Table 1.

It will be seen that for the total 65 miners tested, the average threshold values in the cases of hysterics, anxiety neurosis and malingerers are the same as for normal mentality, whereas it is higher in manic depressives and in the dull and backward.

In the group of control miners, the psychologically abnormal had a lower threshold than the normal, while in the certified cases the rise in threshold in hysteria and anxiety neurosis was more marked in those without nystagmus than in those with active oscillations.

### Conclusion

The evidence such as it is points to the fact that among miners there is no significant relationship between the psychological state and the threshold of dark adaptation. It would be interesting to compare them with a group of ordinary workmen in this respect.

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## BINOCULAR VISION IN MINERS

BY

DOROTHY ADAMS CAMPBELL, RENEE HARRISON  
and JEAN VERTIGEN

THESE preliminary investigations were made in the hope that a minute study of the behaviour of the eyes under conditions of low illumination might reveal the mode of onset of nystagmus.

The binocular vision of miners was compared with that of a large group of normal subjects of the same age groups:—

(a) in full light adaptation.

(b) in full dark adaptation (after 45 minutes in the dark).

The tests were made on the synoptophore, using test slides calibrated for known illuminations. For tests (a) the illumination

varied from 0.025-0.37 F.C. and for tests (b) from 0.0025-0.18 F.C. Thus in dark adaptation the subject was exposed to a range of illumination comparable to that found at the coal face, but not so low as to exclude foveal vision, except for the stereoscopic test at 1/10 illumination.

*Range of illumination*

	Full Illumination	Grades		
		1/10	1/4	1/2
For Stereoscopic Vision	0.025 F.C.	0.0025	0.006	0.012
Fusion and Ductions	0.22	0.02	0.05	0.11
Simultaneous Perception	0.37	0.04	0.09	0.18
	Light adapted eye	Dark	adapted eye	

Black and white slides were used for the tests, and the calibrations were made photometrically with the slides in position. The illumination recorded was that which fell upon the eye at the synoptophore. The recording scales on the synoptophore were made visible with luminous paint and only a small red torch was used to help the patient get into position after he had completed his time of dark adaptation.

Each subject was tested for stereoscopic vision, fusion, ductions and simultaneous perception—in this order—and was made familiar with the tests in light adaptation before proceeding to full dark adaptation.

Subjects with strabismus were not included in these comparative figures. We were interested to find that quite a number of miners are working happily on the coal face with strabismus but they had no binocular vision, and were presumably free from any mental effort in this respect. There were also men with high degrees of hypermetropia but low visual acuity, also with no binocular vision.

The tests used were suitable for subjects who could see 6/24

and over. A detailed record of the visual acuity has not been made in this report since it was amply proved by Llewellyn in his earlier report on Miners' Nystagmus that the disease does not run concurrently with the error of refraction.

(1) *Observations on Subjects able to perform Binocular Vision Tests.*—(1) It was noticed that in all subjects the subjective angle tends to become convergent when they are dark adapted.

Miners suffering from nystagmus—did not show this phenomenon so markedly, see Table I.

TABLE I. *Variation of subjective angle*

Subjects	No. examined	Light adapted eye			Dark adapted eye		
		Simultaneous Perception (0.37 FC.)	Fusion (0.22 FC.)	Stereoscopic (0.025 FC.)	SP2 (0.04 FC.)	F. (0.02 FC.)	SV. (0.002 FC.)
Normals	72	1.5°	1.4°	0.2°	2.6	3.2	1.5
Miners from Coal Face	32	0.6	0.8	0.9	1.8	2.0	1.5
Miner's Nystagmus	36	1.0	1.0	1.2	0.9	1.5	2.0

As will be seen the subjective angle did not vary directly with the illumination but appeared to depend on the state of the eye—and with the type of visual test.

The majority of miners showed an abnormal fixation—i.e., their eyes tended to look upwards. The older men—experienced giddiness following upon their tests in the dark.

(2) *Stereoscopic vision.*—We were agreeably surprised to find that the majority of the normal population has good stereoscopic vision. Thus in 200 normals—of both sexes, the incidence of subjects with poor stereoscopic vision in ordinary illumination was only about 5 per cent. The incidence was higher than this in the group of controls tested in these experiments, and tended to increase with increasing age—and under conditions of dark adaptation. This variation occurred more in miners, and most markedly in those suffering from nystagmus. (See Table II.)

TABLE II. *A comparison of Stereoscopic Vision at different Illuminations*

Shewing percentage of individuals found to have good stereoscopic vision

## 1—Age Group 25-44

	Total No. tested	Illumination			
		·0025 FC.	·006 FC.	·012 FC.	·025 FC.
Normals	(30)	87%	90%	87%	83%
Control Miners	(16)	50	50	81	75
Miners with Nystagmus	(12)	33	8	17	33

## 2—Age Group 45-54

Normals	(30)	67	70	70	80
Control Miners	(10)	33	50	60	70
Miners with Nystagmus	(17)	32	32	25	32

## 3—Age Group 55-70

Normals	(30)	53	63	70	63
Control Miners	(10)	40	40	40	50
Miners with Nystagmus	(8)	11	22	22	44
		Dark adapted eye			Light adapted eye

(3) *Comparison of Stereoscopic Vision with Adduction.*—In the synoptophore tests performed as for distance vision it was evident (see Table III) that:—

TABLE III. *Comparison of Adduction (average angle) in subjects of all ages (25-70).*

With good stereoscopic vision

	Illumination			
	0.025 FC.	0.05	0.11	0.22
Normals	18°	16°	16°	17°
Control Miners	21°	20°	21°	19°
Miners $\bar{c}$ Nystagmus	18°	18°	19°	13°

With poor stereoscopic vision

Normals	14°	14°	12°	13°
Control Miners	10°	7°	5°	8°
Miners $\bar{c}$ Nystagmus	4°	5°	4°	4°
	Dark adapted eye			Light adapted eye

- (a) The power of adduction is normal—subjects did not vary with illumination.
- (b) Subjects having poor stereoscopic vision had practically the same power of adduction as those possessing good stereoscopic vision.
- (c) Miners (both nystagmus subjects and “control” miners from the coal face) who had good stereoscopic vision, had a noticeably greater power of adduction than normals.
- (d) Miners of both types—with poor stereoscopic vision, had hardly any power of duction at all.
- (4) *Nystagmus*.—It is known that certification for miner's nystagmus on clinical grounds does not rest on the existence of actual nystagmus. Indeed, in long-standing cases, particularly in those subjects who have been off work for a long period—no actual nystagmus can be elicited—and the outstanding features are photophobia, blepharospasm and a psychological abnormality which obviate the performance of any binocular vision test.

In the intermediate stage where bilateral nystagmus is present, any attempt at macular fixation results usually in macular suppression, though some degree of fusion, duction and stereoscopic vision are present.

In the early stages of the disease, nystagmus can be unilateral and is usually vertical. Some show vertical nystagmus in one eye and horizontal in the other—while one interesting individual showed alternating macular suppression of great rapidity, while he still possessed good duction, fusion and stereoscopic vision, and developed no actual nystagmus. He was unable to continue his work but improved rapidly with rehabilitation.

Quite a number of miners have been seen who complained of headache and giddiness and occasional oscillations. They showed no nystagmus either by clinical tests or on the synoptophore, but had some degree of suppression in one eye—and poor duction. Their symptoms were improved by orthoptic training.

### Conclusions

Up to the present time cases of miners' nystagmus have not been seen by ophthalmic surgeons—until their symptoms are long-standing. They have then developed so marked a psycho-neurosis, that the secondary symptoms far outweigh the original nystagmus. The patients frequently find it impossible even to read 6/60 on account of blepharospasm—and the ophthalmic surgeon has dubbed them hopeless from the point of view of any treatment which he could give them. He has been inclined to suggest that the nystagmus arises from voluntary convergence.

It must not be forgotten that the evidence of previous observers is that defective illumination is the primary cause of miners' nystagmus. My observations during the past three years point to a breakdown in binocular vision under conditions of low illumination. It is only by a minute analysis of the various processes involved that any theory of the origin of nystagmus can be promulgated. It would appear that macular vision is a separate entity—which proceeds independently of the more primitive functions—of fusion, of fusion with duction, and of stereoscopic vision. The latter can certainly be maintained even in low degrees of visual acuity—and is I think (Campbell, 1947) much more likely to depend on the rapid alternation of monocular impressions, brought about by small fusional movements of the eyes (see Clark, 1946), than by summation of stimuli from the two eyes. Burian (1939), (1941) has in fact shown that any disturbance of fusion in the paramacular area will distract macular vision and cause a separation of foveal images. If this is true for the light adapted eye one wonders what occurs in conditions of low illumination.

Many other points require explanation, *e.g.*, as to why nystagmus usually gives rise to intolerable symptoms about the age of presbyopia, and (b) as to the effects of posture on the function of the extra-ocular muscles. These are to be the subject of later experiments together with an analysis of the binocular vision under such low illumination that the fovea cannot respond.

We wish to record our thanks to the Medical Research Council for a grant towards the expense of these investigations.

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### SLIT-LAMP MICROSCOPY\*

BY

J. H. DOGGART

LONDON

IN the years that immediately followed the first world war, a great deal of enthusiasm was aroused in these islands by the work of Vogt and others with what was then a novelty—the slit-lamp and corneal microscope. A number of British ophthalmologists went on pilgrimages to Switzerland, fired by ambition to equip themselves with knowledge of the new weapon. It was perhaps only natural that these crusaders should become intoxicated by the thrilling new world of phenomena unfolded before their eyes, and we need feel no surprise that some of them launched into extravagant claims. They even suggested—greatly to the consternation of the non-crusaders—that evidence given in a Court of Law by ophthalmic surgeons could not thenceforth be regarded as expert unless it included facts derived from slit-lamp observation. Here was a chance for the enemies of the new toy, as they derisively dubbed the slit-lamp. “What is the use,” they asked, “of all this pampering and bottle-feeding? You will only succeed in producing a generation of ophthalmologists unable to see anything without the help of intricate and costly devices.” Another upholder of traditional methods was heard to say: “Show me

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something that I can't already see with my loupe, and then I'll begin to consider peering down those new-fangled tubes."

Now that we are once again passing through the aftermath of a world war, it seems fitting to review the status of slit-lamp microscopy, and the chances of arriving at a reasonable estimate of its value should be brighter than they were in the 1920's, because the instrument is no longer a novelty, and the words already written by its devotees run into millions. In the first place, however, it will be necessary to mention some of the main objections urged by the opponents of slit-lamp microscopy. Then we must ask: "To what extent are these objections justified?" Next we should consider how the beginner can avoid the fallacies and abuses which do admittedly arise from injudicious use of the slit-lamp. Afterwards it will be possible to summarise the chief benefits to be gained from using the instrument, but the problem will be easier to understand if that summary is preceded by a brief account of the evolution of technique.

Turning then to the clinical details, let us consider the importance of recognising certain benign varieties of pre-senile cataract. Finally, metallic impregnation of the structures accessible to slit-lamp microscopy will come under notice together with the colour-changes induced by non-metallic agents.

### 1—Main objections to slit-lamp microscopy

Many ophthalmologists have argued that the high cost of a slit-lamp renders it a useless luxury for all except research workers, because the lower ranges of magnification are ample for routine work, so long as the observer has been adequately grounded in his specialty. Moreover they can quote instances of serious conditions unrecognised by the volatile microscopist, though his old-fashioned colleague had no difficulty in detecting them with a loupe. Furthermore the slit-lamp enthusiast is accused of raising unnecessary scares. Early iridocyclitis, and even sympathetic ophthalmia, we are told, have been wrongly diagnosed on the score of a few stray pigment granules settled on the back of the cornea, or floating about in the anterior chamber.

With a few unimportant exceptions, they go on to say, the phenomena revealed by slit-lamp microscopy can perfectly well be appreciated by means of focal illumination and the monocular loupe; and the main result of using higher magnifications is to blunt the faculty of perception, so that the microscopist will be seriously handicapped when he has to do without his beloved machine, as, for instance, in examining a bed-ridden patient. Another alleged disadvantage is that the ordinary work of an out-patient department is delayed by slit-lamp enthusiasts laboriously

searching for minutiae. Finally it is pointed out that the teaching programme is already overburdened, and that instruction in slit-lamp microscopy is bound to curtail the time available for more important methods of investigation.

## 2—Comments upon the foregoing objections

Concerning the expense of the instrument, we may retort that a good slit-lamp will last for many years if it is properly tended, and the running costs are negligible. It must be conceded that a slovenly clinician undergoes no miraculous transformation, merely by virtue of gazing down a microscope, and clearly we shall obtain far more valuable guidance from a sound ophthalmologist without knowledge of the slit-lamp, than an unskilled observer could give us with the aid of the most elaborate machine. If, however, an instrument is to be judged by the errors of its least experienced wielders, what methods of examination will remain at our disposal? Gigantic blunders are perpetrated every day with the ophthalmoscope and the perimeter, and many a large keratic precipitate has escaped detection through a loupe. Nor is the raising of unnecessary scares a monopoly of slit-lamp enthusiasts. Indeed this instrument has been known to allay scares by contradicting the sinister impressions derived from a loupe.

It will presently be shown that the number of phenomena revealed by the slit-lamp but hidden from the loupe is not negligible, and it is certain that, although access to higher magnifications may blunt the perceptive faculty of some, yet others are thereby stimulated to seek more detailed information with their loupe, when once the finer changes have been revealed by slit-lamp microscopy. With regard to the argument of out-patient delay, it may be replied that most of the cases in ordinary practice do not need to be scrutinised with the slit-lamp, and that the extra time required for examination of suitable ones will be negligible, so long as the observer has gained facility in rapid focusing. Finally the use of the instrument can be rapidly taught to anyone with moderate intelligence and a grounding in elementary ophthalmology. One recognised item in such grounding is the scrutiny of histological specimens, fragments of dead tissue which have been plunged into a succession of protoplasmic poisons, as well as being transformed by aniline dyes. The student then proceeds to look at inverted images of these mutilated, meretriciously coloured fragments with the aid of a monocular microscope. Every ophthalmic surgeon is deeply indebted to the pioneers of morbid histology, whether he knows it or not, but recognition of this debt should not prevent us from wondering why some of the experts in that branch of medical science should have seen fit to discourage the inspection

of living eyes under relatively slight magnification, with the aid of a binocular instrument furnishing an erect image.

### 3—Discrimination in slit-lamp microscopy

In order to avoid some of the pitfalls which beset the path of a beginner, the student of slit-lamp microscopy should constantly bear in mind two sources of fallacy. First is the mistake of interpreting harmless phenomena as pathological. Secondly the signs that may be manifested in a number of different conditions have been described as pathognomonic of one disease.

One good example of the first mistake was supplied by slit-lamp novices who solemnly diagnosed ariboflavinosis in hundreds of people who merely exhibited the normal vascular loops at the limbus. Another instance—whose consequences would have been more serious if the patient had accepted the original advice—was furnished by the surgeon who advocated excision of an eye alleged to be suffering from melanotic sarcoma of the iris. In that particular case the real condition was senile atrophy of the mesodermal stroma, whereby the pigment layer was left exposed over a sector of the iris. Other obvious examples are *slight* aqueous flare, and peripheral bedewing of the corneal epithelium. Both of these physiological phenomena have undergone sinister interpretations in the mind of the tyro.

Unfortunately there is no sovereign recipe to prevent such mistakes, but the slit-lamp observer is more likely to keep a sense of proportion if he resolves to regard the instrument not as a means of escape from the simpler methods of examination, nor yet as a slot-machine designed for snap-diagnosis, but rather as an accessory weapon, which can be exploited in certain cases only—and not even then, except in co-operation with the older methods of attack. In the first place, therefore, let the microscopist be familiar with the normal anatomy of the eye, and especially of its anterior segment. Knowledge derived from naked-eye study of anatomical specimens and scrutiny of histological slides must be correlated with the facts of physiology and with the results of observation upon the living-eye with and without the aid of lower magnification. The binocular or monocular loupe, or both, should always be exploited before we resort to slit-lamp inspection, and it is essential to examine hundreds of eyes in order to recognise the range of difference within normal limits, as well as the harmless congenital defects and atrophic manifestations which have so often been misinterpreted as danger-signals.

With regard to the mistake of imagining non-specific signs to be pathognomonic of one particular disease, many instances are enshrined in the literature. Conjunctival varices have been

wrongly accepted as conclusive evidence of old injury by mustard-gas. Syphilis has been held responsible for patches of iris atrophy among people free from venereal disease. Many of the generalisations confidently propounded by early workers in this field have been disproved by the growth of knowledge, and it would appear that the best way to guard against false assumptions of pathognomoncity is to acquire wide clinical experience—including *pooled* experience, so that obscure and difficult cases can be illuminated by free discussion.

#### 4—Evolution of the apparatus

Let us now consider the main landmarks that mark the advance of technique in slit-lamp microscopy. It is nearly fifty years since Czapski succeeded in obtaining erect images by the incorporation of prisms in a binocular microscope. Further improvements in this instrument were designed by Zeiss, but its utility could not fully be exploited until a method was devised for concentrating light upon the object under scrutiny.

This problem of adequate illumination was simplified by the slit-lamp which Gullstrand demonstrated at the 1911 International Congress of Ophthalmology. Light from a homogeneous Nernst filament was focused by a system of lenses upon a slit, so as to constitute a secondary source of light, which could in its turn be concentrated upon the structure under examination by means of a condensing-lens balanced in the observer's hand. So long as the remainder of the room was kept moderately dark, Gullstrand's apparatus enabled any part of the anterior segment of the globe to be displayed in striking contrast with the unlit neighbouring tissues.

Five years later the patient's comfort and the convenience of the observer were promoted by Henker's device, whereby the slit-lamp and the illuminating lens were both mounted upon the same articulated metal arm. Thus he secured the advantages of steadiness and mobility, making it possible to survey details in more leisurely fashion.

Gullstrand found himself handicapped, at the close of the first world war, by inability to obtain the Nernst lamp. The Nitra lamp, which he adopted as a substitute, consisted of a spiral filament of tungsten, so that the light focused in the slit was no longer homogeneous. It consisted of a bright image of the filament, and the same spiral source of confusion was evident at the focal portion of the beam passed onwards by the illuminating lens. Nevertheless Gullstrand learned to ignore this image of the filament when he wanted to use the focal part of the beam. Moreover he began to exploit the pre-focal and post-focal portions, in which the light was homogeneous.

The next advance was due to Vogt, whose inventiveness was spurred by his dissatisfaction with Gullstrand's method of illuminating the eye. By moving the lamp forward, he contrived that the slit became full of homogeneous light. Homogeneous also became the focal portion of the beam, when the illuminating-lens exerted its focusing power upon this secondary source of light. One result was a more-than-fifty per cent. increase in the intensity of illumination, but another and more important advantage accrued. The method of optical section was rendered possible.

Under Gullstrand's system of illumination the spiral image only filled a portion of the fully-extended slit, so that the light was little influenced when the aperture underwent moderate contraction. Further narrowing soon reduced the efficiency of the illumination without offering any compensatory increase in the distinctness of structures under observation. If, on the other hand, the homogeneous strip of light which fills the slit under Vogt's system of illumination is constricted, it not only retains its brilliance, but also permits the appreciation of details difficult to discern under the brilliance of the wider beam. Thus certain architectural features of the lens are thrown into relief, and accurate judgments concerning the depth of corneal lesions facilitated.

One minor supplementary device consisted of a blackened tube between the slit and the illuminating-lens, designed to trap scattered light which else would dazzle the patient and confuse the observer. Another useful aid was obtained by transmitting the light through a small circular hole instead of the slit. The resulting conical beam shows up stray particles floating in the aqueous, or enables us to appreciate abnormal degrees of opalescence in that medium.

Perhaps the most important step of recent years has been the harnessing of slit-lamp methods to gonioscopy. It will be remembered that Trantas tried to explore the secrets of the anterior chamber with the aid of his ophthalmoscope nearly fifty years ago, at the time when Czapski was achieving erect images with his binocular microscope. Then Salzmann carried the work onwards with the aid of a contact glass, making numerous discoveries in spite of his primitive apparatus. Koeppe, Troncoso and others afterwards began to use various types of monocular microscope in conjunction with a contact glass. Several observers in the 1920's made attempts to enlist the aid of the binocular corneal microscope, but no simple and satisfactory technique was evolved until the problem was attacked by Goldmann.

In 1938 Goldmann devised an adjustable contact glass providing a ninefold magnification, and fitted with a mirror in which could be scrutinised an image of the anterior chamber lit by the slit-

lamp. This method enabled the patient to be examined sitting at the slit-lamp in the same way as for ordinary microscopy of the eye. Under the older systems of gonioscopy the patient had to be lying down, and the technique was relatively cumbersome; but Goldmann made it possible for examinations to be swiftly undertaken in the course of the out-patient clinic, and without any need of any additional equipment besides the adjustable contact-glass. He soon found that many gonioscopic problems were simplified by varying the width of the slit during examination of the chamber-angle. His next refinement was to incorporate a special camera in the apparatus.

#### 5—Advantages to be gained from slit-lamp microscopy

When it is used with discrimination, the slit-lamp can supply valuable help in the following aspects of ophthalmology:

(1) *Diagnosis.* There are certain forms of disease whose earliest stages cannot be detected without recourse to the slit-lamp. Fuchs' so-called epithelial dystrophy furnishes a good example, because the first signs of this malady implicate the endothelium, whose mosaic design cannot be seen with a loupe. It can only be appreciated by slit-lamp examination in the zone of specular reflection. The slit-lamp also permits absolute certainty concerning certain features which cannot be authoritatively established under smaller magnification. We can, for instance, answer the question whether a corneal scar has penetrated the whole thickness of that membrane. Admittedly the correct answer is in many cases obtainable by means of a loupe and focal illumination, but there is a certain proportion of cases in which the issue can only be decided with the aid of the slit-lamp.

(2) *Prognosis* must, of course, be intimately linked with diagnosis, because obviously we cannot offer a reasonable forecast unless we recognise the nature of a given lesion. Careful study of the differential morphology of lenticular opacities will enable us in a large proportion of instances to indicate whether an opacity is stationary or progressive. In the case of a progressive opacity, it will often be possible to say whether the advance is likely to be slow or rapid. Similarly in corneal lesions a careful survey of the depth, situation, size and shape of the opacities, together with the presence and disposition of adventitious vessels and the state of the fellow-eye, will often enable us to predict the likely outcome, so long as these phenomena are studied in the light of previous clinical experience.

(3) *Treatment.* Unfortunately the cases in which the slit-lamp is likely to be most useful in establishing an early diagnosis are only too often examples of incurable conditions, such as corneal

dystrophy of unknown origin. Therefore slit-lamp microscopy cannot always give a positive lead in the matter of treatment. It can, however, supply warnings against unnecessary or harmful remedies, which have so often been applied by reason of mistaken diagnosis. Further the effects of treatment stand a greater chance of being accurately assessed, especially in cases of iridocyclitis, because of the detail in which the anterior segment of the eye can be viewed.

(4) *Academic research.* Although this aspect is mentioned low down on the list, because the present lecture is mainly intended for clinicians, yet it must be emphasised that no sharp distinction separates academic from other kinds of slit-lamp microscopy. The recognition of embryological vestiges and aberrations of development concerns—or should concern—the practising ophthalmologist as closely as it does the academician.

#### 6—Benign forms of pre-senile cataract

Insults to the well-being of the lens, whether they arise from sudden violence, from malnutrition, toxic substances or the slow deterioration of old age, produce one common result—impaired transparency. When opacity has spread to involve the whole structure, we speak of *total* or *mature* cataract, and it is not always possible for the observer to deduce what was the main initial provocation; but unfortunately we find a different set of conditions in cases of *partial* cataract. Certain types of opacity display characteristic morphological grouping, or exhibit a predisposition for special layers of the lens fibres. Some follow a typical series of steps in their progress towards maturity. Others remain stationary. It is in these cases of partial cataract that we can gain so much from the cumulative experience of older clinicians, because there is no self-evident feature, such as would permit sharp, radical distinction between the benign dot and the flake which heralds total cataract. Differentiation is largely empirical.

Some forms of partial cataract are intrinsically beautiful when we see them with the aid of the microscope under the slit-lamp's concentrated beam. Embryologists gain additional delight from the apt way in which these opacities may illustrate various stages in development. From the standpoint of clinical practice, however, there are two main facts that must be borne in mind. In the first place, lack of knowledge concerning the differentiation of partial cataracts has often been responsible for the delivery of a needlessly bad prognosis. Secondly, such ignorance has led to erroneous opinions concerning the causation of certain cataracts. Thus it is clearly desirable, for medico-legal as well as purely medical reasons, that ophthalmologists should strive to distinguish between



the various types of cataract. Admittedly we cannot attain absolute certainty in every instance, but certain we can be in a large proportion of cases, and, where some doubt exists, we can at any rate offer opinions in an ascending scale of probability, if only we learn how to detect the relevant details.

(1) *Anterior capsular cataract* in its pure form is a rarity, and most of the cataracts so-called implicate some superficial lens fibres as well as the capsule. Pure capsular opacities are of minute size, and exhibit around their circumference an unshagreened halo when they are examined in the zone of specular reflection.

(2) *Anterior capsulo-lenticular cataract* is often situated at the axis of the lens, in which case it is described as an *anterior polar cataract*. Strands of persistent pupillary membrane are often found anchored to the front of these opacities, and another commonly associated feature is a bunch of epicapsular stars, which can easily be identified by their slender branching processes.

(3) *Anterior axial embryonic cataract* is the name given to any irregular collection of opacities situated near the anterior Y-shaped suture, which marks the front of the foetal nucleus.

(4) If the opaque dots are disposed in such a way as to map-out the anterior or posterior Y-shaped sutures, or both, we speak of *suture cataract*.

(5) *Floriform cataract* is a less common condition, in which the limbs of the anterior Y may show an efflorescence of petals.

(6) *Dust-like cataract in concentric layers* is the somewhat cumbersome title given to dots scattered at different levels of the lens.

(7) When dots of opacity are confined exclusively or chiefly to the foetal nucleus, we speak of *cataracta centralis pulverulenta*.

(8) *Coronary cataract* is present in at least 20 per cent. of young adults, but remains undetected in a large proportion of cases, because the opacities are chiefly situated towards the periphery of the lens, which is not exposed to view until the pupil is dilated. The most characteristic opacity is club-shaped, and each club usually displays an expanded end pointing toward the axis of the lens. Associated opacities, chiefly in the form of round dots and biconcave discs are always present, and may be coloured green, blue or yellow, as well as white. Cholesterin crystals are another common finding.

The subject of coronary cataract may, of course, come to exhibit superimposed signs of senile cataract by the time he reaches an age that renders him liable to the latter condition, but, so far as the coronary opacities are concerned, he should not be exposed to a discouraging prognosis. Many authentic cases are on record in which excellent vision was enjoyed more than twenty years after

this form of cataract had been originally noted. It seems abundantly clear that this type of opacity advances so slowly that it does not constitute an appreciable menace to sight. The other above-mentioned varieties are even more benign, being practically stationary. None of them is likely to entail any appreciable impairment of vision, except those instances of anterior capsulo-cuticular cataract which encroach sufficiently upon the axis to obstruct the victim's view.

### 7—Metallic impregnation

Characteristic changes arise in certain structures of the eye as a result of impregnation with metals, and it is interesting to note that these substances may gain access to the globe in a number of different ways. Intra-ocular metallic foreign bodies are one obvious source, but changes may also occur from the implantation of metallic dust scattered by certain industrial processes. Another possible origin is the therapeutic use of metallic salts, either in the form of local applications, or systemically administered. The metals now to be considered are iron, copper, gold, mercury and silver.

(1) *Iron* is responsible for the halo of rust which so commonly surrounds metallic fragments embedded in the cornea, but this form of staining disappears soon after removal of the foreign body. If, however, a steel or iron particle is retained for many months inside the globe, characteristic pigmentary changes develop. The corneal substance shows an orange or yellow tint, more marked at the periphery than at the axis. Rustiness of the iris offers a striking contrast with the colour of the unaffected fellow-eye in cases of siderosis. Generalised atrophy of the lens is betrayed by blurring or effacement of the zones of discontinuity, and the anterior epithelial cells, especially at the equatorial region, are pricked out in a cluster of brownish dots. Moreover the whole lens is tinged yellow, with a noticeable deepening of tint at the anterior band. As a rule the vitreous displays broken bundles peppered with reddish granules.

(2) The changes provoked by *copper* are most clearly evident when the intra-ocular foreign body is very small. Larger fragments are apt to incite a destructive reaction before the characteristic changes have had time to unfold. The cornea exhibits a vivid blue coloration of Descemet's membrane, most intense in the neighbourhood of the limbus, and fading towards the axis. Often it will be found that only a portion of the thickness of the membrane is implicated. Some observers have reported a reddish-brown stain in the same situation, but all the instances seen by the writer were blue.

In the lens we find sunflower cataract, which consists of a thin layer of opacity situated immediately behind the anterior capsule, and characterised by an axial disc from which petals jut outwards in the manner suggested by its name. The usual colour of a copper cataract is greyish-blue, and its most striking feature is a brilliant polychromatic lustre in the zone of specular reflection. Greenish vitreous fragments are sometimes visible. Cases of chalcosis from copper medication have been described by several authors, and Butler (1929) reported corneal changes in a polisher of copper, although, he located the blue coloration in the deeper layers of the substantia propria, not Descemet's membrane.

(3) *Gold* salts employed in the treatment of tuberculosis were held responsible for a peculiar pigmentation of the cornea in a case described by Bonnet and his colleagues (1936, 1937, 1939). On the anterior surface of Descemet's membrane they found minute grains of gilt associated with a brilliant lustre.

(4) Lenticular changes from absorption of *mercury* were reported by Atkinson (1943), who surveyed 70 patients occupationally exposed to mercury vapour. Slit-lamp microscopy showed at the level of the anterior capsule a coloured reflex, with its maximum intensity in the pupillary area. Among different subjects the tint varied from light brownish-grey to deep rose-brown, and in some instances the reflex was interrupted by round holes or irregular cracks reminiscent of defects in the silvering of a mirror. Atkinson came to the conclusion that ocular hydrargyrosis must be an early manifestation of mercurialism, because a number of his cases were symptom-free, and manifested no other signs of impregnation with mercury.

(5) *Silver* nitrate and the various organic silver preparations, e.g., argyrol and protargol, impart a slate-grey stain to the conjunctiva after prolonged instillation. Associated corneal changes, so far as the writer's experience goes, consist of (a) grey or grey-green discoloration of the peripheral zone of Descemet's membrane, and (b) broken reticulation in the deeper layers of the corneal substance. Some authors have described a golden coloration of Descemet's membrane. Others have mentioned a blue change in that layer. It may well be that the same metal in different chemical combinations may convey various tints to one particular tissue. Another possibility is that a patient may unwittingly mislead the surgeon, and omit to mention that he had been treated with some other preparation, e.g., copper-stick as well as silver-containing drops.

Corneal argyrosis may also result from endogenous medication, as recorded by Ascher (1924), in a woman whose anti-syphilitic treatment had consisted of silver-salvarsan injections. A number

of different observers have also mentioned peripheral coloration of Descemet's membrane among silver-foundry workers. The conjunctiva seems to remain unstained, except in those who have been in the habit of rubbing their eyes with fingers contaminated with silver. Larsen (1927) reported a greenish punctate deposit immediately behind the anterior capsule of the lens, as well as greenish-gold lustre of Descemet's membrane. Bischler's (1942) case of occupational argyrosis in a silver-engraver showed more pronounced changes in one eye than in the other, but the deepest pigmentation was consistently peripheral.

### 8—Other pigmentary changes

The expression "pigmentary change" is often taken to mean change consisting of a black or brown coloration of the structures concerned, but it is proposed now to extend the signification of "pigment" so as to embrace all conspicuous changes in colour. Although this section is primarily concerned with non-metallic pigmentation, it may as well be admitted at the outset that iron-containing products derived from the breakdown of haemoglobin may be responsible for some of the conditions presently to be described.

Before we proceed to consider instances of definite pigmentation, it is worth while to emphasise that some of the signs evident on slit-lamp microscopy must be accepted with a pinch of salt. In other words the optical conditions are in many respects illusory. Thus, for instance, oedematous corneal epithelium viewed under retro-illumination may appear brown, simply because the reflecting screen in that particular case happens to be a brown iris. Furthermore we may find that certain lenticular opacities take on a different tint, according to whether they are viewed under direct or indirect illumination. Which is the real colour? Of course all colour is real, in the sense that it represents a subjective experience. On the other hand, common-sense insists on discriminating between sensations artificially isolated in the laboratory, and the evocative experiences of ordinary life.

Superficial pigmentary lines, whose exact composition has not yet been demonstrated, are exemplified by *Hudson's line*, which is not uncommonly found in the lower half of a hitherto healthy cornea. Similar markings may be found in association with any longstanding opacity, whether the latter was a consequence of trauma or of inflammation. A broken ring of superficial pigment is also characteristic of conical cornea.

Scattered pigment granules on the back of the cornea, or entangled in the iris stroma, or clinging to the anterior capsule of the lens are common features of an elderly eye, because the

pigment layer of the iris constantly disintegrates as time goes on. Occasionally such granules are concentrated on the posterior surface of the corneal axis to form a Krukenberg's spindle, especially in myopes. Coloured crystals are sometimes found in connection with old corneal scars. Superficial blood-staining may arise from rupture of an adventitious corneal vessel, but the expression "blood-staining of the cornea" is usually reserved for those cases where hyphaema in association with raised intra-ocular pressure leads to prolonged changes in the substantia propria. In reality the successive shades of brown and green developing in such corneae are not due to blood itself, but rather to an invasion of the substance by haemoglobin derivatives. These products pass through Descemet's membrane from red corpuscles undergoing disintegration in the anterior chamber.

The Kayser-Fleischer ring consists of closely-set golden granules occupying a part of the thickness of Descemet's membrane at the corneal periphery. It is a constant feature of Wilson's disease, or hepato-lenticular sclerosis.

Anomalies and irregularities of iris pigmentation are commonly found on routine examination. Clumps of pigment cells in the stroma constitute benign melanomata, and can be found in a majority of the subjects examined. Total congenital heterochromia is rare, but a sector of differently coloured stroma is by no means uncommon. Deepened pigmentation of the stroma is usual in the neighbourhood of congenital ectropion of the uvea. Hyperpigmentation and verrucosity of the stroma is a self-explanatory term. In heterochromic cyclitis the affected iris acquires a washed-out blue colour, and it is interesting to note that the keratic precipitates laid down in the course of this disease usually remain grey, in contrast with the brownish hue acquired by old precipitates deposited during other kinds of iridocyclitis.

Pigmented deposits upon the anterior capsule of the lens include congenital epicapsular stars, scattered granules from disintegration of the posterior layer of the iris, and larger clumps of iris pigment left sticking to the capsule after mydriatics have pulled an inflamed iris away from the axial region. Vossius' ring consists of pigment granules imprinted upon the capsule by sudden backward thrust of the iris, the result of aqueous compression from the impact of a blow upon the eye. In most instances the ring undergoes spontaneous absorption within a few weeks. Senile exfoliation of the zonular lamella may produce pale-blue debris in the peripheral region of the anterior capsule.

The senile lens usually exhibits a pronounced golden glow in the zone of specular reflection near the level of the posterior capsule. Not uncommonly we find a faint play of colours,

especially in connection with the cupuliform variety of senile cataract, but this phenomenon should not be confused with the true polychromatic lustre of a complicated cataract, because the latter exhibits comparatively large and vivid splashes of colour, alternating with each other in a manner reminiscent of differently coloured countries on a map. Coloured crystals are a frequent finding in the type of cataract associated with Mongolian idiocy, cretinism, or dystrophia myotonica. We have already noted that suture-cataract may be coloured blue, yellow or green, and the same applies to dilacerated opacities, and to the club-shaped and other elements of a coronary cataract.

Brownish granules entangled in the cobweb-like framework of the vitreous are a normal feature, as may be ascertained by any one who looks at vitreous protruding into the anterior chamber after the operation of capsulotomy for after-cataract. In old age the broken vitreous bundles may be profusely sprinkled with granules resembling brick-dust. The non-crystalline opacities that constitute synchysis scintillans are usually white, but coloured cholesterol crystals are occasionally found in cases of injury, or as a consequence of non-traumatic haemorrhage and exudates, retinal detachment or intra-ocular neoplasm. In many instances of Eales' disease we find nothing but whitish curds in the vitreous, even though preliminary focal illumination has led us to expect otherwise, by reason of a pronounced red glow coming back through the darkened pupil. There may, however, be clumps of red blood corpuscles adhering to the posterior capsule of the lens.

### General conclusions

When the teaching of slit-lamp microscopy was beginning to spread through the world of ophthalmology in the 1920's, many of its devotees maintained that no further problems were likely to be solved by the scrutiny of microscopic sections. One result of this attitude was to multiply mistakes which might have been avoided if the information gained from slit-lamp microscopy had been correlated with facts assembled by generations of morbid anatomists. Now that another quarter-of-a-century has elapsed, many an eager surgeon would like to relegate slit-lamps as well as monocular microscopes to the rubbish-heap. The main field of description has been so thoroughly mapped-out, especially by Vogt in his brilliantly-illustrated—and unobtainable—encyclopaedia, that the chances of a new clinical entity being discovered by the average ophthalmic surgeon are indeed small. Meanwhile the process of acquiring technical facility with the slit-lamp does demand a certain amount of intelligent concentration, and offers no spectacular rewards.

It is therefore inevitable that many of the younger ophthalmologists are turning to radiology and biochemistry in the hope of finding an answer for their unsettled problems. Wonder-drugs and the magic of vitamins, haematological data of ever-increasing complication, and elaborate X-ray photography, are only a few of the present-day requirements for treating and investigating the bewildered patient. Of course all these advances are desirable, in so far as they are applied with discrimination and with due regard to the facts established by older methods. What must be stressed, however, is the vital necessity of careful routine examination by instruments capable of being handled without summoning the specialists from half-a-dozen other departments. Admittedly we must try to maintain close relations with other kinds of specialists, and, more important still, with the family practitioner and the general physician, but it is quite certain that such contact will be far more fruitful if we do our share of gathering the relevant facts.

In conclusion it is suggested that the slit-lamp has been abundantly proved to be a valuable weapon for the practising ophthalmologist, especially in the realm of diagnosis. At the present time, however, the accumulated facts of slit-lamp microscopy are in danger of being neglected, with consequent loss of clinical accuracy. The table upon which the instrument rests is normally flanked by two stools—one for the patient and one for the observer. Is it not perhaps true, metaphorically as well as literally, that the slit-lamp has fallen between two stools? On the one hand it has suffered the sidelong glances of many an older clinician, whose apprentice-days were completed before the slit-lamp era. On the other hand is the rising generation eager to sharpen a new set of weapons. All success to them—and to their patients!

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This paper contains numerous references to the various forms of metallic impregnation of the cornea.

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## POST-OPERATIVE INTRA-OCULAR INFECTION CONTROLLED BY PENICILLIN \*

BY

F. S. LAVERY

DUBLIN

AS cases which develop intra-ocular infection following upon cataract extraction almost invariably do badly I am reporting the following case which, as a result of using penicillin, has proved an exception to the rule.

J. D., aged 65 years, had a combined extra-capsular extraction done on his right eye on September 27, 1947. Although there was some cortical remains no wash-out was employed. The appearance of the eye was satisfactory until four days later when the cornea became hazy and the iris presented a muddy appearance. He was put on sulphadiazine tablets, four as an initial dose, and two four-hourly as maintenance dose. Penicillin drops (5000 units per c.c.) were instilled hourly. Next day the condition of the eye showed a marked deterioration. There was pus in the anterior chamber and the wound edges were infected. 50,000 units of penicillin were injected sub-conjunctivally, and 500,000 intra-muscularly every four hours. The sub-conjunctival injections were repeated on the two days following, and the intra-muscular injections were continued for four days. On the third day after the first sub-conjunctival injection of penicillin the condition of the eye showed a marked improvement. The wound edges were now healthy and the pus had been absorbed from the anterior chamber. He was discharged from hospital four weeks from the date of operation. The eye was quiet. The projection of light was accurate, and it is expected that capsulotomy will give him good vision in the eye. When the patient was re-admitted in December, 1947, it was found that a capsulotomy was not required, the corrected vision in the eye being 6/6.

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\* Received for publication, November 4, 1947.



## ANNOTATION

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### Wiping the Eye

The elderly, who often have relaxed lower eyelids, tend to have a small accumulation of fluid between the lid and the globe which may in time lead to epiphora. Such people should be advised to wipe the eye from the outer canthus inwards towards the nose in order to maintain as far as possible the position and tone of the lid; for if the lid is forcibly wiped downwards or outwards from the nose it tends to keep up a vicious circle. But it must be confessed that it seems to be more natural to wipe from within outwards.

Besides this topical allusion the phrase wiping the eye has an idiomatic meaning. When any one makes a mistake and has it pointed out to him by a more alert colleague, the latter is said to have wiped the other fellow's eye. It must be confessed that we all make mistakes, we should not be human if we did not. Some make more than others. In our early student days everyone must have been astounded at the amazing intuition of our teachers in diagnosis. The worst of "Aeneas" is that he's always right was once said of a physician well known to the writer. But "Aeneas" was not infallible. We often wonder whether those giants of the past, Bowman, Hutchinson and Nettleship ever had their eyes wiped? We recall asking a much respected teacher of our's how it was that he never seemed to miss anything. His reply was, "my dear boy if you only knew of the things I miss, you would be surprised."

If the legislature were to issue a decree that eyes in future must not be wiped it is certain that most of us would lose a great deal of enjoyment. There is always a feeling of satisfaction in the man who, *e.g.*, removes a speck from the cornea or conjunctival sac after some one else has assured the patient that no foreign body was present. The feeling varies with the temperament of the wiper; some experience a mild satisfaction, others, an unholy gusto.

A patient may come to consult you on account of failing vision and you find that chronic glaucoma is present. He says that he has been aware of some difference in his sight for about a year and that two years ago he was all right and was examined by another oculist who found nothing wrong. We do not consider there to be any justification at all in thinking that you have wiped the previous oculist's eye. Early signs may have been present and not discovered, or they may not. We do not know enough to be certain. Nor should the man who finds 0.25 D. of astigmatism present in a presbyope who is wearing a low spherical correction for reading assume that the man who ordered the glasses was not aware of the astigmatism. Such an attitude seems to be quite unjustifiable.

But when you are called to see a case that a general practitioner has been treating with atropine for a week under the assumption that iritis was the condition when it really was glaucoma, you are certainly justified in considering that you have wiped the G.P.'s eye. It is unfortunate if those in general practice who have had no special training in ophthalmology get the idea that atropine drops can be used indiscriminately in ophthalmology. It would be much better if they would confine their prescriptions to simple boracic lotion and call in a consultant early.

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## CORRESPONDENCE

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### SOLAR RETINITIS

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—The article on "solar retinitis" by Emanuel Rosen which appeared in your January number is a notable contribution to this subject, and will probably interest those of your readers familiar with cases of solar injury as much as it interested me. The outstanding feature of the article is the observation that one or more holes at the macula were noted in a series of 23 cases of solar injury tabulated in detail, and that holes at the macula were seen in over 500 undetailed cases of coloured troops "every one of whom was exposed to the direct action of the sun's rays."

Many other interesting points are evoked, however, some of which you may perhaps allow me to raise here, *viz.* :

1. Has the author seen many cases in which the typical early appearances resulting from sun-gazing, direct or indirect, was not followed by an actual hole, and in which complete recovery apparently took place?

2. What is the frequency with which the typical appearance of the sun-gazer's macula (such as described by Kirkpatrick in Elliot's *Tropical Ophthalmology* and quoted at length by Dr. Rosen), occurs when the unprotected eye is exposed to prolonged tropical glare when "working out of doors, etc.," but not subjected to direct sun rays or rays reflected from a glazed surface? H. E. Smith, quoted by the author, seems to consider such a sequence of events is relatively frequent.

3. What are the similarities and differences in early and late appearances between the typically produced sun injury at the macula, and the so called central serous and central angiospastic retinopathies, supposed to be associated with disturbances of the autonomic nervous system? Is the immediate effect of the sun

injury a minute serous or haemorrhagic bleb which takes a variable time to burst (or absorb without bursting), and the late effect ordinarily a hole?

4. If a hole at the macula following solar injury is relatively common in tropical and subtropical environments, and it probably is, what is the frequency with which it is followed by detachment of the retina?

5. To what extent are dark skinned races less liable to sun injury at the macula?

6. Why do some individuals escape who look directly into the sun again and again in the course of practising a religious rite, or of performing a duty such as taking an observation on the sun at sea, whether they be fair skinned or dark skinned, whilst others suffer the characteristic damage?

It would require access to many case records and to a voluminous literature to discuss profitably some of the questions asked above, and go far beyond my first intentions in writing this letter. I shall therefore content myself with a few remarks, and opinions based for the most part on memory.

If a hole (or holes) at the macula is as frequent a sequel to the sun-gazing trauma as Dr. Rosen's observations indicate, why has the positive diagnosis of hole not been made more often in tropical ophthalmic clinics, and in the clinics of other countries after eclipses? The reason I think is, that in order to be quite certain that the sharply marked maroon coloured spot is or is not a hole, it is essential to employ adequate specialised illumination. Dr. Rosen used retro-illumination (method of Friedenwald). Vogt, by means of red-free light, determined details at the macula previously unobserved. Elliot knew that a hole might occur, so did Kirkpatrick, yet in the Madras Ophthalmic Hospital the usual diagnosis of the typical lesion was, "sun injury at the macula" or some such. I was seldom quite satisfied that a solar trauma had produced a hole until, shortly before leaving Madras in '37, I started using the Friedenwald hand ophthalmoscope with slit illumination and filters. The ordinary British hand ophthalmoscopes used in routine work were unequal to the exhaustive clinical examination of macular detail. I imagine that with suitable apparatus and illumination the diagnosis of hole at the macula would often augment that of solar injury, by obviating dependence on parallax.

With regard to (1) above my opinion is that complete recovery of vision and complete (?) normality of macular appearances may follow a typical sun-gazer's macula with diminished visual acuity and central scotoma. Complete is queried since the observations on which this opinion is founded were made with the ordinary electric ophthalmoscope. In considering (2), one must be very careful to avoid introducing a fallacy. After a considerable experience of the fundus

appearances met with in South India, both in Europeans and Indians whose eyes were unprotected from tropical glare, I do not remember having seen a case of sun-gazer's macula in which exposure to direct sun rays, or sun rays reflected from a glazed surface, was excluded. The possibility of the injury being caused by rays reflected from sheets of water such as one finds in the paddy fields of South India was well recognised; but there are very many other ways in which an indirect solar injury may be caused. One case (records 1924), which eluded me at first, was that of a surveyor who took a bearing on a heliotrope with a theodolite. I shall be surprised if a good case is made out for the thesis of H. E. Smith to which the author alludes, if I interpret this correctly from his reference.

A consideration of (3) would lead us too far afield.

With regard to (4), a prolonged follow-up of cases would be necessary to determine this point. Detachment following hole at the macula, however, is said to be rare whatever its aetiology. I cannot remember seeing a detachment associated with sun injury at the macula; but then I have seen relatively few Europeans with this affection, and my impression is that detachment of the retina, from whatever cause, is much more uncommon in the Indian eye.

The answer to (5) requires two strictly comparable series of figures, which are not at my disposal. In considering (6), the duration of exposure is presumably very important. Possibly the refraction plays a part. I formed impression that myopes were less liable to sun injury at the macula, but have no records to support this. In a series of 21 cases which I published with Dr. Venkatarangum Nayudu after the 1922 eclipse no record was made of the refraction, and since then the detailed records of my cases are not available. Dr. Rosen's series shows a preponderance of hypermetropes.

Dr. Rosen considers that the danger of solar injury is not sufficiently recognised by the medical profession and the community at large. This is probably true for certain parts of the world, but even in those parts of the tropics where sun-gazing is practised as a religious rite or takes place unintentionally during agricultural employment, and is relatively common and well recognised, the damage to sight does not appear to be so severe as to place it amongst the more important causes of preventible amblyopia. It would probably be a great mistake for the average European to become too glare conscious when living in the tropics and for the ophthalmologist to overstress the risk of sun injury, however attentive to the comfort and idiosyncrasies of the individual patient perturbed by conditions associated with excessive light.

Yours sincerely,

ROBERT E. WRIGHT.

FLEET, HANTS.

February, 7, 1948.

## TRAVELLING SCHOLARSHIPS

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRs.—There are many reasons why the fortunes of British ophthalmology are temporarily at a low ebb: some of them are entirely honourable and many of them are beyond our control. But there are two lines of practical policy which may be pursued to regenerate our specialty. One is the long term policy of organised research and the other is shorter, taking full advantage of the benefits of foreign study.

Organised research is getting under way: the Research Chair of the Royal College of Surgeons of England has already enabled research work to attract international interest and in due course the Ophthalmic Institute of the University of London will place ophthalmic research in this Country on a broad foundation. The work being done over the Border needs no mention from me.

Foreign study, however, is a more urgent policy of replenishment and, in my opinion, it should be pursued now and with the utmost vigour, before our plans of re-organisation are too far advanced. By publishing his experiences in Switzerland, John Foster (*Brit. Jl. of Ophthal.*, Vol. XXXII, No., 2, February, 1948) has done a great service to his colleagues and has clearly shown the way which should be followed. As a result of following his trail, made easy by much generous advice, I should like to offer the following suggestions which will enable young ophthalmologists up and down our land to share the enormous professional and cultural benefits which are to be obtained by visiting foreign clinics.

Travelling scholarships should be immediately instituted. They should be awarded by a responsible body to British ophthalmologists of considerable experience who are not over the age of 40 years. Such a scholarship would enable a student to spend a short period of study at clinics anywhere and not more than two clinics in any country should be visited by one student so as to spread the opportunities as widely as possible.

An essential feature of this scheme should be that on return home the scholar should give a detailed report on the work of the clinics he has visited, by lecturing to his colleagues. Think what a feast could be provided on a winter's evening by listening to the reporters recently returned from Swiss, Dutch, Russian or United States clinics!

Money is available and temporary Government restrictions will not daunt the President of our Faculty.

Although most desirable, organised tours do not fulfil quite the same serious purpose which I have in mind, nor do they give the foreign host the opportunities he would wish to have for discussing

individual problems in detail or demonstrating individual methods. Reports from accredited individuals would keep British ophthalmologists constantly informed of the changes in ophthalmic fashions abroad. "Experience" has been defined as the practice of the same mistake a hundred times: it is experience of this kind which we in this country can well do without and the surest way to avoid it is to watch the other fellow at work either at home or abroad.

With the aid of such delightful craftsmen as the Grieshaber family and the Haag Streit combination, the vast experience of Swiss ophthalmologists has set a high standard of international achievement. To have shared a little of this experience, offered with such grace and courtesy, is something for which I and many others shall always be grateful. It is in the hope that others may be enabled to do the same that I ask permission to occupy your valuable space with my plea for action forthwith.

Yours faithfully,

B. W. RYCROFT.

149, HARLEY STREET, W.1

February 13, 1948.

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## RESIDUAL CATARACT

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*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRs.—The remnants of the lens left behind after the extra-capsular cataract extraction or the discission operation are known as the "after cataract" or the "second cataract." Both of these terms would appear unsatisfactory on closer examination. Moreover, the second one is confusing, since the text-books too often use the term "secondary cataract" to connote the "complicated cataract" as well as the "after cataract."

I would beg to suggest, for the consideration of the ophthalmic world, the term "residual cataract" for this condition which is essentially a lens residue, although in the production of which the proliferation of the sub-capsular epithelium and sometimes the pigmentary, haemorrhagic and inflammatory elements enter.

Yours truly,

J. N. TOLIA.

4, CARLINGFORD ROAD,  
LONDON, N.W.3.

January, 12, 1948.

## OBITUARY

## PHILIP H. ADAMS

By the death of Philip Adams on February 9 an association with Oxford Ophthalmology of nearly fifty years is severed. After leaving Lancing in the late 'nineties he came up to Exeter College, Oxford, and during his period there as an undergraduate spent much time working at the Oxford Eye Hospital as a clinical assistant to his uncle, Robert Doyne, and for some part of this time filled the post of unqualified house surgeon there. After taking his degree and first M.B., he went to the London Hospital for clinical experience. While at the London he qualified M.B., Oxon, and in 1904 took the F.R.C.S., (Eng.). He then returned to Oxford and started ophthalmic practice in partnership with Robert Doyne, and was appointed Assistant Surgeon to the Oxford Eye Hospital.

The period 1900/1910 was a very active one in Oxford Ophthalmology. A Readership in Ophthalmology had recently been established with Doyne as the first Reader. The Diploma in Ophthalmology was inaugurated and the beginnings of the Oxford Ophthalmological Congress were in the making.

Into all these activities Adams entered to the full, and it can be said that the subsequent success of the Congress was largely due to his efforts, inspired by the genius and drive of Doyne and backed by the business and literary ability of Sydney Stephenson.

In 1912 on the retirement of Doyne, Adams was made Reader in Ophthalmology to the University and Senior Surgeon to the Hospital.

From then on for thirty years he was the lynch pin of Oxford Ophthalmology. He was responsible as Deputy Master for a large part of the arrangements for each annual Congress at the Oxford end; as Reader he was responsible for the course of study needed by Statute for candidates for the Diploma of Ophthalmology, and he was at the same time, as Senior Surgeon to the Hospital, involved in day to day affairs relative to its efficiency. He also had a large private practice. He carried out all these manifold duties with great efficiency, but in a most self effacing manner. It would have been hard for anyone not knowing him intimately to guess the amount of work he shouldered.

He went through the post of Master of the Oxford Ophthalmological Congress for the period 1925/1927, and he delivered the Doyne Memorial Lecture in 1931. In 1944/1945 he was President of the Ophthalmic Section of the Royal Society of Medicine.

As a clinician, Adams was quite outstanding, showing much shrewdness in diagnosis and in managing patients. As an operator he was in the highest class.



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PHILIP H. ADAMS

*Elliott & Fry*





SIR H. LINDO FERGUSON

*The Acme Photo Co., Dunedin*

He had great charm of manner, and a most distinguished and handsome appearance. He was always immaculately turned out.

Adams retired from Oxford in 1941 and had made a home in the Eastern Counties, but he attended the Congress each year and it is a sad thought that we shall not see him there again.

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### SIR H. LINDO FERGUSON

By the death of Sir Lindo Ferguson on January 22, at Dunedin, New Zealand, the Ophthalmological Society of Great Britain lost its sole surviving foundation member.

Sir Lindo was born in London in 1858. His family moved to Ireland and, in 1873, at the age of 16, he entered the Royal College for Science of Ireland with a Royal Scholarship. He graduated in chemistry and then, turning to medicine, entered Trinity College.

After completing his arts course, he trained at Adelaide Hospital, qualified at the age of 22 and went into residence at St. Mark's Ophthalmic Hospital. After a period of study on the Continent, he held assistantships at various ophthalmic departments and, in 1883, he obtained his Fellowship of the Royal College of Surgeons of Ireland and graduated Doctor of Medicine at Trinity College.

Soon afterwards, for reasons of health, he travelled to New Zealand, and, finding an embryo medical school in Dunedin, decided to practise there. At this time he was the only ophthalmic surgeon in New Zealand or Australia and very soon his opinion and services were asked for from all quarters. In 1884 he opened the ophthalmic department at Dunedin Hospital and was appointed Lecturer in Ophthalmology two years later. For fifty-two years Sir Lindo served on the staff of the Hospital, always enjoying the esteem of his colleagues, his students and his patients. In 1914 he was appointed Dean of the Medical Faculty, and, realising that the rapidly growing Medical School was woefully lacking in accommodation, he set about the task of rebuilding. Years of hard work for Sir Lindo followed, and 1927 saw the Departments of Anatomy, Physiology, Pathology and Bacteriology all housed in a building which stands as a monument to him.

For twenty years he was a professional representative on the Otago University Council and for eight years a member of the Senate of the University of New Zealand. He was a foundation member of the Ophthalmological Society of the United Kingdom, an original member of the Royal Academy of Medicine in Ireland, an Honorary Fellow of the American College of Surgeons, a Foundation Fellow of the Australasian College of Surgeons, a member of the New Zealand Medical Council and a past President of the New Zealand Branch of the British Medical Association. He was Patron of the New Zealand Ophthalmological Society, founded in 1947.

Outside his profession he was interested in all good causes, but his chief interest lay, perhaps, in art, and he was President of the Otago Public Art Gallery Association.

In 1918, his work for the community was recognised by the award of the C.M.G., and, six years later, by the bestowal of a Knighthood.

The words of the present Dean of the Otago Medical School sum up the character of one who will long be remembered by his colleagues.

"His contribution to Medical education in New Zealand was monumental, and, for a generation, he gave himself unsparingly, without thought of financial reward, to the leadership of the Medical School. His foresight, wisdom and breadth of vision were instrumental in raising the school from obscurity to its present position. His hospitality and kindness to staff, to students, and to patients were proverbial, and benevolence was the keynote of his nature."

## NOTES

**Appointment** Air Vice-Marshal P. C. Livingston has been appointed Director-General of the R.A.F. Medical Service.

\* \* \* \*

**Edinburgh  
Post-Graduate  
Board for Medicine** A series of post-graduate lectures and clinical demonstrations on Ophthalmology will be held during the period May 17 to May 29, 1948. The class is intended for graduates specialising in this subject, and the number will be limited to a maximum of 20.

The meetings will be held in the Ophthalmic Department of the Royal Infirmary, Edinburgh. Fee, 8 guineas.

Enquiries and applications for enrolment should be addressed to:—The Director of Post-Graduate Studies, University New Buildings, Edinburgh, 8.

\* \* \* \*

**Corrigendum** In Mr. Keith Lyle's letter, March, 1948, p. 191, the last word of the first paragraph should read "therapy," not "surgery," as printed.

\* \* \* \*

**Sociedad de Oftalmologia  
De Guadalojara** This Mexican Society of Ophthalmology was duly constituted on November 27, 1947: among its activities will be an active campaign in the prevention of blindness.

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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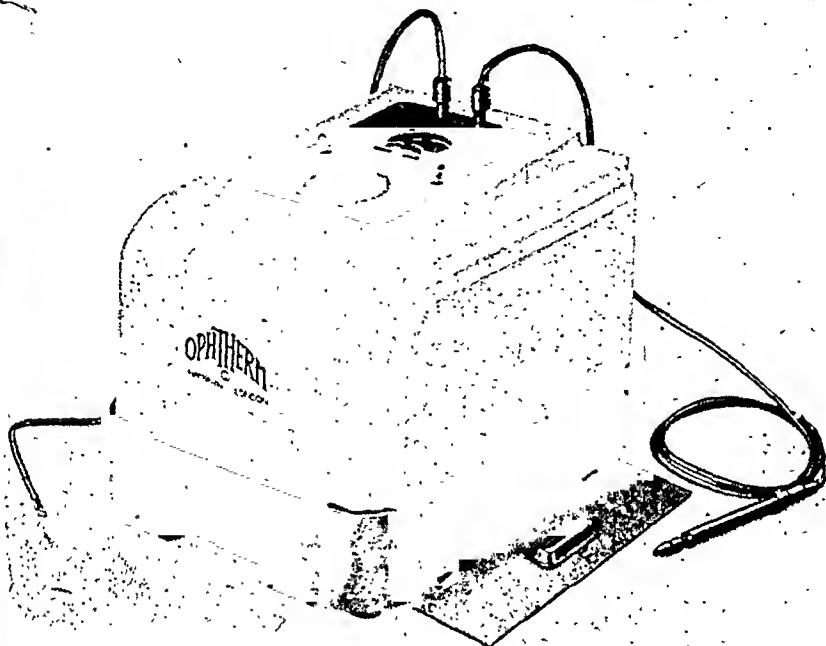
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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

MAY, 1948

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## COMMUNICATIONS

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### THE OPTICS OF CONTACT LENSES

BY

A. G. BENNETT

THE subject indicated by the title of this paper ranges over a wide field, but only that part of it which is of significance to prescribers has been dealt with here. An attempt has been made to present the subject matter as simply as possible without detriment to precision. Gaussian methods in particular have been avoided wherever they appeared unnecessary. On the other hand, attention is drawn to some commonly neglected factors which are of importance in contact lens prescribing.

#### 1.—Neutralising the cornea

The idea of contact lenses was apparently conceived by Sir John Herschel after reading Airy's account of the correction of his own astigmatism by means of a sphero-cylindrical lens.

Herschel, though admiring Airy's ingenuity, evidently thought this too indirect a way of overcoming what he termed "malconformations of the cornea" and suggested instead a "spherical capsule of glass" filled with animal jelly and applied to the cornea. Thus the contact lens was first conceived as a means of re-moulding the cornea, or, expressing it more accurately, of building it up into a truly spherical surface, the function of the glass shell being purely mechanical and not optical.

Completely to neutralise the anterior surface of the cornea would require a fluid medium of the same refractive index as the corneal substance, namely 1.376, whereas the refractive index of all the solutions at present in use is slightly lower, being about 1.336. Since, for a given radius, the power of a surface is proportional to the refractivity (refractive index minus unity) of the medium, it follows that the fluid neutralises only  $336/376$  or approximately nine-tenths of the anterior power of the cornea. It will hence be realised that the effect of corneal irregularities or deformities is not completely counteracted.

The extent to which a contact lens neutralises corneal astigmatism is not a simple matter to determine. If we accept the constants of Gullstrand's No. 1 Schematic Eye as a basis for discussion, the following picture emerges. The corneal radii are 7.7 and 6.8 mm. respectively, its centre thickness 0.5 mm. and its refractive index 1.376, the index of the aqueous humour being 1.336. From this it can be calculated that the anterior surface of the cornea has a power of +48.83D., and the posterior surface of the cornea a power of -5.88D., the ratio of these two powers being -8.3:1.

Now if the corneal astigmatism is ascribed to its anterior surface only, it would follow as before that the fluid meniscus will correct nine-tenths and leave one-tenth uncorrected. If, on the other hand, both surfaces of the cornea are assumed to be toroidal with their meridians of maximum curvature in similar orientation, then the astigmatism due to the posterior surface will annul a portion of that due to the anterior surface. Suppose, for example, that both surfaces of the cornea exhibit the same percentage difference between the two principal radii, then since the surface powers are in the ratio -8.3:1, it follows that the posterior surface will neutralise nearly one-eighth of the astigmatism created at the first surface. The fluid lens neutralising nine-tenths for its own part, there would thus be a very small degree of over-correction.

One further point is worthy of mention. In order to make some allowance for the posterior surface of the cornea, keratometers are calibrated for an empirical refractive index of 1.3375.

For example, the dioptric reading corresponding to a radius of 337.5 mm. is  $\frac{337.5}{7.7} = +43.83\text{D.}$ ; whereas taking the true index of 1.376 the corresponding power is  $+48.83\text{D.}$

As a result, the reading given by a keratometer represents, in actual fact,  $337.5/376$ , or very nearly nine-tenths of the power of the anterior surface. Similarly, the "corneal astigmatism" as measured by the keratometer represents in reality nine-tenths of the astigmatism due to the front surface only. The keratometer is incapable of giving reliable information as to the total corneal astigmatism. To accept its reading involves the assumption—which may or may not be justified—that the posterior surface is a replica of the anterior, with its principal meridians identically orientated, and its principal radii both reduced to approximately nine-tenths of the corresponding radii of the anterior surface.

## 2.—The Effectivity relationship

The optical theory of contact lenses cannot be adequately expounded without reference to the principle of effectivity, which deals with the change in the dioptric vergence of a pencil of rays over a given length of its path. (The vergence  $L$  dioptries at a given point is defined as the reciprocal of the distance  $l$  metres from the given point to the origin or focus of the pencil.) In passing it may be recalled that the first detailed exposition of

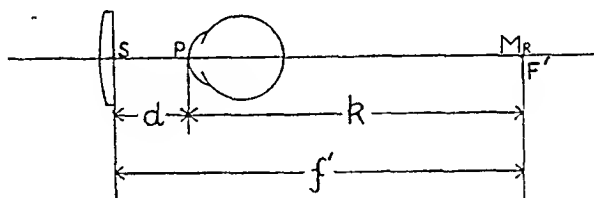


FIG. 1.

Spectacle and ocular refraction.

geometrical optics based on the idea of vergences was due to Sir John Herschel, who used the term "proximity" to denote the reciprocal of linear distance.

As an illustration we may take the relationship between spectacle and ocular refraction, which assumes some importance in contact lens prescribing. Fig. 1 represents a hypermetropic eye with its far point at  $Mr$ . In everyday practice, the refractive error is invariably expressed in terms of the correcting lens



which, placed at the "spectacle point"  $S$ , renders the eye emmetropic. The second principal focus  $F'$  of this lens must coincide with the far point. Its power  $F$  dioptres, the reciprocal of the focal length  $f'$  in metres, is termed the spectacle refraction. The distance in metres from the corneal vertex (more strictly, from the eye's first principal point) to the far point  $M_r$  is usually denoted by the symbol  $k$  and its reciprocal  $K$  is termed the ocular refraction. If the vertex distance from the spectacle point to the cornea is  $d$  metres, it is clear from the diagram that  $k = f - d$  and hence

$$K = \frac{1}{k} = \frac{1}{f-d} = \frac{F}{1-dF} \dots \dots \dots (1)$$

$K$  represents the back vertex power of the contact lens required to correct an ametrope whose spectacle correction is  $F$ . By "contact lens" is meant, in this connection, the system comprising the glass or plastic shell and the liquid lens combined.

In general, a pencil with a vergence  $L$  dioptres at a given point will have the vergence  $L_d$  after travelling a distance  $d$  metres in air where

$$L_d = \frac{L}{1-dL} \dots \dots \dots (2)$$

If the pencil is travelling in a medium of refractive index  $n$ ,  $d$  in this expression must be replaced by the "reduced distance"  $d/n$ . We shall need to make further use of this effectivity expression.

(The symbols and sign convention employed in this paper are those standardised by the Northampton Polytechnic Institute, London, E.C.1, and the Imperial College of Science.)

### 3.—Theory of afocal lenses

The first spherically ground lenses to be made available were produced by Carl Zeiss and were based on the Herschelian idea of reshaping the cornea. The glass lens itself was afocal in air. It is important to have a precise definition of this term; to say that it denotes a lens or system "without power" is not sufficient. An afocal lens is a lens without power with respect to infinitely distant objects; that is to say, a parallel pencil incident at the first surface emerges as a parallel pencil from the second. Such a lens does exert a focal effect with respect to near objects. That this distinction is not purely academic will emerge at a later stage.

Although the centre thickness of any contact lens is necessarily small, it is not so in comparison with the radii of curvature and, consequently, thin lens formulae cannot be used without introducing serious errors. Take, for example, a lens with a posterior corneal radius of 8 mm. and centre thickness 0.6 mm., the refractive index of the material being 1.5. If the front surface were also ground to a radius of exactly 8 mm. in accordance with thin lens theory, the resulting lens would be far from afocal: its back vertex power would be no less than +1.60D.

The precise relationship between the radii of curvature of an afocal lens is easily found. Denoting the radii by  $r_1$  and  $r_2$  respectively, the centre thickness of the lens by  $t$  and the refractive index of the material by  $n$ , the two surface powers  $F_1$  and  $F_2$  are given by the text-book formulae

$$F_1 = \frac{n-1}{r_1} \quad \dots \quad \dots \quad \dots \quad (3)$$

$$\text{and} \quad F_2 = \frac{n-1}{-r_2} \quad \dots \quad \dots \quad \dots \quad (4)$$

$r_1$  and  $r_2$  being in metres.

If we now imagine a parallel axial pencil incident at the front surface, its vergence after refraction will clearly be equal to  $F_1$ . After travelling a distance  $t$  metres towards its focus, its vergence will be increased to

$$\frac{F_1}{1 - \frac{t}{n} F_1}$$

in accordance with the effectivity formula. Hence, if the pencil is to emerge parallel, *i.e.*, with zero vergence, after refraction at the second surface, the power  $F_2$  of the latter must be such that

$$\frac{F_1}{1 - \frac{t}{n} F_1} + F_2 = 0$$

$$\text{whence} \quad F_1 + F_2 - \frac{t}{n} F_1 F_2 = 0 \quad \dots \quad \dots \quad (5)$$

The above may be followed more easily by reference to Fig. 2, which indicates the vergence of the pencil before and after each refraction.

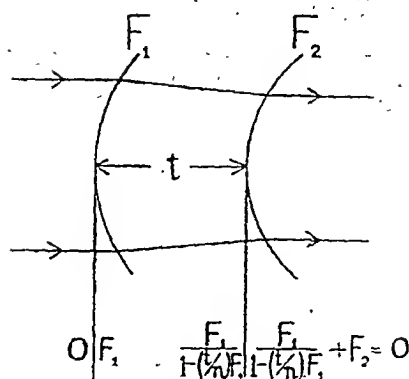


FIG. 2.

Passage of light through an afocal lens. The vergences are shown before and after each refraction.

The left-hand side of the last equation will be recognised as the formula for the equivalent power of a thick lens. The equation can be re-arranged in the form

$$F_1 = \frac{-F_2}{1 - \frac{t}{n} F_2} \quad \dots \quad (6)$$

showing the necessary relationship between the two surface powers of an afocal lens. To obtain the relationship in terms of radii, we replace  $F_1$  by  $\frac{n-1}{r_1}$  and  $F_2$  by  $\frac{n-1}{-r_2}$ , as above, and thus arrive at the equation

$$\frac{n-1}{r_1} = \frac{\frac{(n-1)}{r_2}}{1 + \frac{t}{n} \cdot \frac{n-1}{r_2}}$$

which simplifies to

$$r_1 = r_2 + \left( \frac{n-1}{n} \right) t \quad \dots \quad (7)$$

Hence the radius of curvature of the front surface of an afocal lens must always exceed that of the rear surface by  $\left( \frac{n-1}{n} \right) t$ .

It can similarly be shown that in order to produce a contact lens with a given back vertex power, the required value of  $r_1$  can

be found by adding  $\left(\frac{n-1}{n}\right)t$  to the value yielded by thin lens theory.

The correction of ametropia with an afocal contact lens is entirely dependent upon the fluid meniscus, which is bounded by the posterior corneal surface of the contact lens (radius  $r_2$ ) and the anterior surface of the cornea itself (radius  $r_c$ ). It hence becomes necessary to determine the value of  $r_2$  which will impart the required power to the fluid lens. An approximation to this value may be found as follows.

Considering the liquid lens as a separate entity and ignoring its centre thickness for the sake of simplicity, its power  $F$  is given by the thin lens formula

$$F = 1000 (n-1) \left\{ \frac{1}{r_2} - \frac{1}{r_c} \right\}$$

$r_2$  and  $r_c$  being expressed in millimetres. Assigning to  $n$  the usual refractive index of 1.336 this expression becomes

$$F = \frac{336}{r_2} - \frac{336}{r_c}$$

Since the liquid lens is in contact with the cornea, its power  $F$  must be made equal to the ocular refraction  $K$ . Hence we may write

$$K = \frac{336}{r_2} - \frac{336}{r_c}$$

$$\text{or} \quad \frac{336}{r_2} = K + \frac{336}{r_c} \quad \dots \quad \dots \quad \dots \quad (8)$$

Having calculated  $K$  from the spectacle refraction and measured the corneal radius on the keratometer, we can thus ascertain the required value of  $r_2$ .

Assuming, however, that the keratometer has its dioptric scale calibrated for a refractive index of 1.3375 in accordance with standard practice, the power  $C$  of the cornea as recorded on the instrument will be equal to  $337.5/r_c$  and hence we may substitute  $C$  for  $336/r_c$  in equation (8) without introducing serious error. We thus obtain the following simplified expression

$$r_2 = \frac{336}{K + C} \quad \dots \quad \dots \quad \dots \quad (9)$$

The literature of contact lenses contains various graphical representations of this formula.

It should be pointed out that formula (9) is only approximate because it does not take into account the thickness of the liquid lens. This point would be worth further discussion were it not for the fact that the fitting of afocal lenses is no longer a commonly practised technique.

Its abandonment was largely due to the resulting conflict between optics and haptics. It can readily be calculated from formula (9), taking an average value of  $+43D$ . for the power of the cornea, that the correction of ocular ametropia over the range  $+12D$ . to  $-12D$ . requires afocal lenses with inner corneal radii varying from 6.1 to 10.8 mm. Indeed, at one time Zeiss afocal lenses were available with radii 5 to 11 mm. in half-millimetre stages. When it is realised that a lens with a 5 mm. corneal radius has a maximum corneal aperture of 10 mm., whilst a lens with 11 mm. radius cannot possibly clear an average cornea, one wonders how such lenses were ever made with any hope of a successful fitting.

It may be added that there is no virtue whatever in making contact lenses afocal and relying entirely upon the liquid lens for the correction of ametropia. From an optical standpoint it is quite immaterial how the total refractive power is divided between the lens itself and the fluid meniscus, whilst from the manufacturing standpoint a perfect afocal lens is certainly no easier to make than any other. On the contrary, small errors in power and defects of surface figure, waviness and so on, are more easily detected in an afocal lens than in one incorporating a refractive effect.

#### 4.—Lenses with added power

Owing to the difficulties briefly alluded to above, it is now the usual practice to select the shallowest standard curve that will clear the cornea and to incorporate any additional power that may be required in the lens itself. Since even small variations in the fluid thickness may have an appreciable focal effect, it is important that refraction should be carried out with the patient wearing a contact lens identical in regard to its back surface and overall size with the lens that is finally to be worn. If any alterations are made, an attempt should be made to estimate their effect on the thickness of the fluid meniscus so that an appropriate allowance can be calculated.

The optical problem is illustrated in Fig. 3. The patient is presumed to be wearing either a semi-finished moulded lens or else a standard trial lens of the appropriate specification, and is found to require an additional power  $D$  at a distance  $d$  from

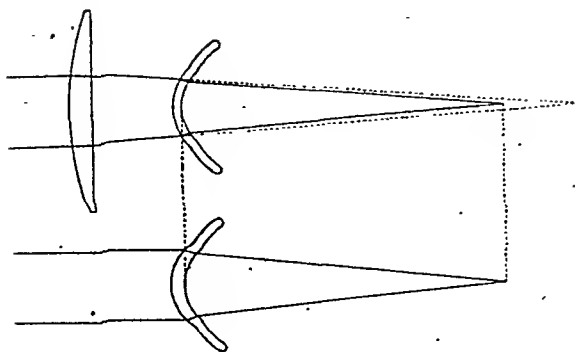


FIG. 3.

Basic optical requirement. The finished lens must have the same back vertex power as the trial contact lens and auxiliary spectacle correction.

the vertex of the contact lens. If the back surface of the latter is identical with that of the lens to be finally worn, the fluid meniscus will be the same in each case. It follows, therefore, that the back vertex power in air of the final lens must be made to coincide with that of the original system in air if it is to have the same effective power at the cornea:

The back vertex power  $F'_v$  of the system can be calculated as follows. Suppose the power of the auxiliary lens is  $+10D.$ , the vertex distance  $d$  12 mm.; and that the contact lens worn during refraction is afocal with a posterior corneal radius of 8 mm.; centre thickness 0.6 mm. and refractive index 1.5. According to formula (7) the corneal radius  $r_1$  of the front surface is given by

$$r_1 = r_2 + \left( \frac{n-1}{r} \right) t = 8.00 + \left( \frac{0.5}{1.5} \right) 0.6 = 8.20 \text{ mm.}$$

Substituting in (3) and (4), the two surface powers are therefore  $500/8.20$  and  $500/-8.00$ , giving

$$F_1 = +60.98D. \text{ and } F_2 = -62.50D.$$

We can now find the back vertex power of the system by tracing through it a parallel pencil of rays incident on the auxiliary lens. After refraction by this lens, the pencil emerges with a vergence of  $+10D.$  and travels 12 mm. or 0.012 metres in air before meeting  $A_1$ , the front vertex of the contact lens. In accordance with the effectivity formula (2), the increased vergence of the pencil at  $A_1$  will be

$$\frac{+10}{1 - 0.012 \times 10} = \frac{+10}{0.88} = +11.36 D.$$

Thus the 12 mm. air space has increased the effective power of the trial lens by  $+1.36D.$  However, as pointed out above, an

afocal lens is without power only in respect to infinitely distant objects and we must therefore proceed to trace the pencil through it.

After refraction by the front surface of the afocal lens, the vergence becomes  $+11.36 + F_1 = +11.36 + 60.98 = +72.34\text{D}$ . The pencil now travels 0.6 mm. through a medium of refractive index 1.5 before meeting  $A_2$ , the back vertex of the contact lens. Hence, again applying the effectivity formula, the vergence at  $A_2$  is

$$\frac{+72.34}{1 - \frac{0.006 \times 72.34}{1.5}} = +74.50\text{ D.}$$

Finally, after refraction by the back surface, the pencil emerges with a vergence of  $+74.50 + F_2 = +74.50 - 62.50 = +12.00\text{D}$ . This gives us the back vertex power of the system, and the final contact lens to be worn permanently must be made with the same back vertex power in air.

Reference should be made to Fig. 4 (not drawn to scale) in which the vergences of the pencil are shown before and after each refraction.

Repeating the procedure for an auxiliary lens of power  $-10\text{D}$ , with all other particulars as before (see Fig. 5), it will be found

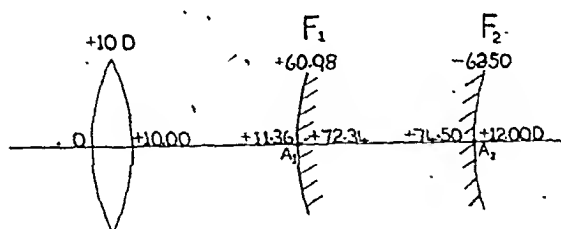


FIG. 4.

Computation of back vertex power: convergent auxiliary lens and afocal contact lens.

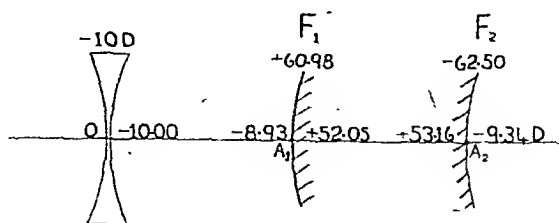


FIG. 5.

Computation of back vertex power: divergent auxiliary lens and afocal contact lens.

that the vergence at  $A_1$  is  $-8.93D.$ , whereas the back vertex power of the system is  $-9.34D.$

Analysing these results we may conclude that the total effectivity correction consists of two portions, one due to the air space or vertex distance and the other due to refraction by the trial contact lens. When the auxiliary lens is of positive power, the two effects are additive; with a negative auxiliary lens they are in opposition.

In the above examples the contact lens worn during refraction has been assumed to be afocal, but exactly the same procedure should be followed in principle whatever its power.

Though difficult mechanically it is theoretically quite simple to incorporate an astigmatic correction in a glass or plastic contact lens. For technical reasons it is usually more convenient to make the inner corneal surface toroidal, in which case allowance must be made for the fact that when filled with fluid the back surface of the lens is partly neutralized. If the refractive indices of the lens material and fluid are  $n$  and  $1.336$  respectively, each dioptré of effective cylinder power will need  $(n - 1)/(n - 1.336)$ , or approximately 3 dioptries of cylinder power worked on the lens itself.

### 5.—Magnification of the retinal image

An exhaustive investigation of this subject on orthodox Gaussian lines has been carried out by J. Boeder.<sup>1</sup> In his paper he deduced accurate formulae which took into account the effects of lens and fluid thicknesses. Unfortunately, one of Boeder's graphs seems to have been drawn upon by other writers, who have failed to study the accompanying text with sufficient care. As a result, a statement is sometimes seen to the effect that in myopia of  $20D.$  contact lenses give a magnification of 46 per cent. In the sense in which it would be ordinarily understood, this statement is not even approximately true.

Supposing an eye to be corrected by a lens placed with its back vertex at a specified distance from the cornea, the size of the retinal image can be varied slightly by altering the form and thickness of the lens. This is, in fact, one of the expedients used in designing lenses for the correction of aniseikon'a. Compared, however, with the change in image size introduced by placing the lens in contact with the eye instead of at the spectacle point, the effects due to form and thickness are of a secondary nature and can thus be neglected in a general discussion. In optical terminology, we shall assume the equivalent powers to be

<sup>1</sup> *Arch. of Ophthal.* (U.S.A.). January, 1938.



the same as the vertex powers. A very much simpler approach to the whole problem is thereby made possible and a Gaussian analysis can be avoided.

First of all we must establish certain definitions. Following Emsley<sup>2</sup> we use the term "Spectacle Magnification" to denote the ratio of the retinal image in the corrected ametropic eye to the blurred or sharp image in the uncorrected eye. With contact lenses it is easily shown (ignoring thicknesses) that the spectacle magnification is in all cases unity.

A graphical demonstration of this fact is given in Fig. 6, which represents a "reduced" hypermetropic eye, the corneal vertex being denoted by P and the macula by M'. Parallel rays are shown emanating from the extremity Q of a distant object situated

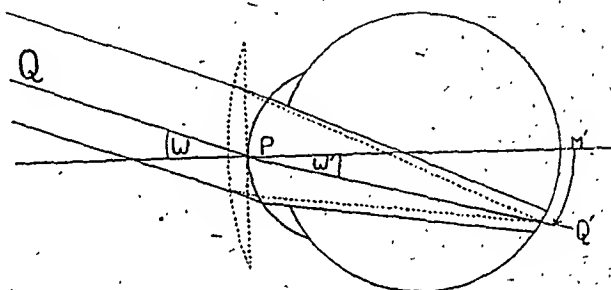


FIG. 6.

Spectacle magnification with a contact lens.

on the axis and making with it an angle  $w$ . The ray incident at P may be regarded as the central ray of the pencil entering the pupil. Hence, if this ray after refraction impinges on the retina at Q', then Q' represents the centre of the retinal blur circle. Furthermore, if the eye accommodates so as to neutralize the refractive error, the sharp image point formed on the retina will still be located at Q'. Thus in either case the size of the retinal image is M' Q'.

Suppose that the eye is now corrected by means of a thin convex lens (shown in dotted outline) placed in contact with the cornea. The central ray QP of the incident pencil passes through the optical centre of this lens and is thus undeviated by it, so that the retinal image point Q' occupies the same position as previously. In other words, the spectacle magnification is unity. The same argument obviously applies to the myopic eye.

The ratio of the retinal image size in the corrected ametropic

<sup>2</sup> "Visual Optics." Hatton Press.

eye to that in the schematic emmetropic eye is termed the "Relative Spectacle Magnification." For any given eye this ratio can be calculated only if the equivalent power of the eye is known. For this reason it is customary to develop two sets of formulae, one applicable to "axial ametropia" and the other to "refractive ametropia." This concept of ametropia as being *either* axial *or* refractive seems to the author altogether too schematic. It means, for example, that an eye hypermetropic 5D. must have a power of either +60D. ("axial" error) or else +55D. ("refractive" error)—no other values being admitted. Most of the published tables giving the "magnification" obtained with contact lenses are, in fact, tables of relative spectacle magnification on the assumption of purely axial ametropia. Although

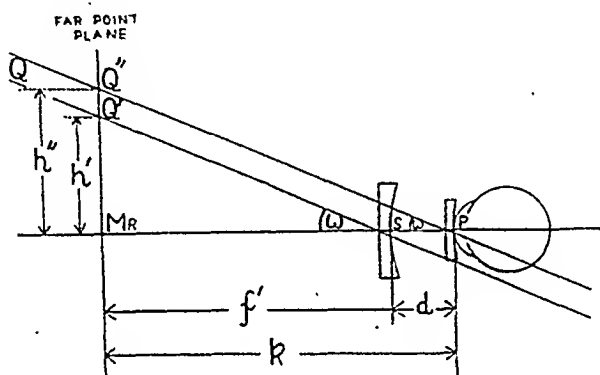


FIG. 7.

Comparison of image sizes in myopia between orthodox spectacles and contact lenses.

giving an indication of theoretical possibilities, their value in practice is questionable.

An exact comparison between orthodox spectacles and contact lenses can be deduced without making any such assumptions. To correct ametropia, a lens must form images of distant objects in the far point plane of the eye. Hence, if lens A forms an image in the far point plane 10 per cent. larger than lens B, the retinal images must also be in the same ratio irrespective of the power of the eye.

Fig. 7 illustrates a myopic eye with its far point at  $M$ , corrected by a lens placed at the spectacle point  $S$ . Parallel rays are shown emanating from  $Q$ , the extremity of a distant object, situated on the axis and making with it an angle  $w$ . Since rays passing through the optical centre of a lens are undeviated, the size  $h'$  of the image formed in the far point plane will be  $M$ .

Q'. If the eye is now corrected by a contact lens, the size  $h''$  of the image  $M_r$  Q'' formed in the far point plane is again determined by the ray passing through the optical centre. By similar triangles it will be apparent that the two image sizes are in the same ratio as the focal lengths of the lenses, i.e.,

$$\frac{h''}{h'} = \frac{k}{f'} = \frac{F}{K}$$

From formula (1),

$$K = \frac{F}{1-dF}$$

Hence 
$$\frac{h''}{h'} = 1-dF \quad \dots \quad (10)$$

Finally, putting  $d$  in millimetres, the percentage difference  $\Delta$  is given by

$$\Delta = \frac{-dF}{10} \% \quad \dots \quad (11)$$

Thus if  $F$ , the spectacle refraction, is  $-20D$ . and the vertex distance 12 mm., a contact lens will give a retinal image 24 per cent. larger than the orthodox spectacle correction.

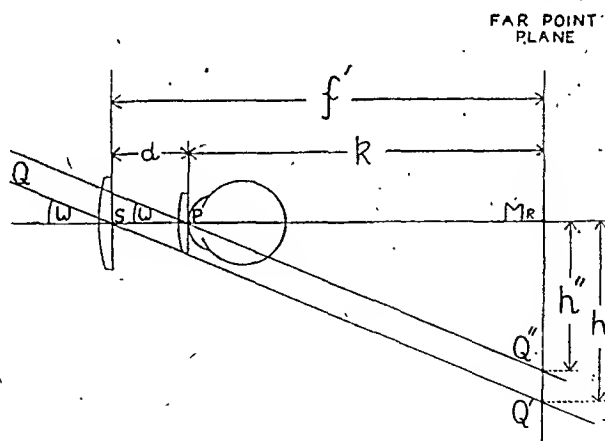


FIG. 8.

Comparison of image sizes in hypermetropia between orthodox spectacles and contact lenses.

Fig. 8 illustrates the position in hypermetropia, from which it will be seen that the same expression holds good. In this case

the smaller retinal image is given by the contact lens, the difference amounting to 7.2 per cent. in hypermetropia of 6D.

### 6.—Contact lenses in anisometropia

Assuming axial errors only, eyes with marked anisometropia will have different retinal image sizes, a fact which may by itself give rise to symptoms. Spectacles placed at the anterior focal points of the eyes would equalise the retinal images. Contact lenses would leave the disparity unchanged. On the other hand, contact lenses have the great advantage of obviating the unequal vertical prismatic effects arising with orthodox spectacles when the eyes rotate to view objects above or below the optical axis.

In unilateral aphakia, contact lenses have the advantage on both counts. The aphakic eye that was previously emmetropic or nearly so has a retinal image about 25 per cent. larger than its fellow, when the correction is worn at 12 mm. from the cornea. Contact lenses reduce this disparity to approximately 9 per cent. and it is stated that binocular fusion has thereby been rendered possible in certain cases.

### 7.—Contact lenses in near vision

Reference has been made above to the relationship between spectacle and ocular refraction. A similar relationship exists between spectacle and ocular accommodation, *i.e.*, between the nominal accommodation reckoned at the spectacle point and the actual effort of accommodation which the eye is required to make.

The left-hand side of Fig. 9 represents a hypermetropic eye corrected by a +6 D. lens placed 12 mm. from the cornea. Parallel rays after refraction by this lens reach the cornea with a vergence of +6.47 D. in accordance with the effectivity formula. In the lower

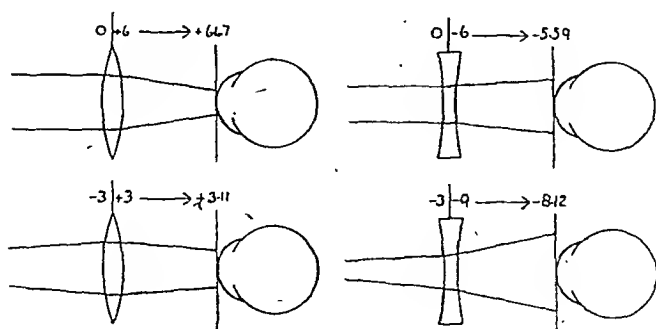


FIG. 9.

Spectacle and ocular accommodation.

half of the diagram, light is imagined to diverge from a point  $33\frac{1}{3}$  cms. or  $-3.00$  D. from the lens. After refraction the vergence is  $+3.00$  D., which is increased to  $+3.11$  D. at the eye as shown. The effort of accommodation required to focus at  $33\frac{1}{3}$  cms. is therefore  $6.47 - 3.11$  or  $3.36$  D. Wearing a contact lens for distance, the accommodation needed to focus at  $33\frac{1}{3}$  cms. from the spectacle point or  $34.5$  cms. from the eye would be only  $2.90$  D.

The position in myopia is illustrated in the right-hand side of Fig. 9, which shows that a myope corrected by  $-6.00$  D. at  $12$  mm. from the cornea has to exert  $2.53$  D. of accommodation in order to focus at  $33\frac{1}{3}$  cms. A greater effort of accommodation would be needed if a contact lens were worn.

### 8.—Sources of error and tolerances

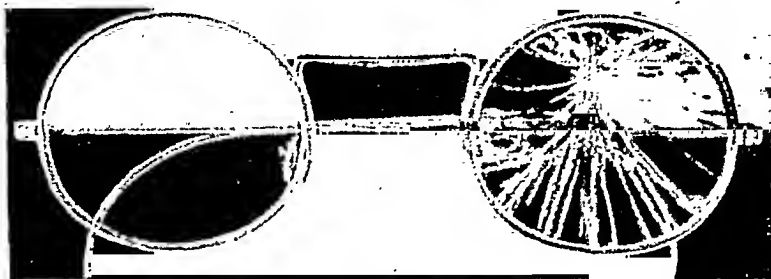
We conclude with a very brief review of possible sources of error in prescribing and manufacturing. Assuming that the back vertex power required has been accurately computed as described above, there are still other factors to be considered. For example, an error of only  $0.05$  mm. in the inner corneal radius of the lens will produce an error in the refractive effect exceeding  $0.25$  D. Again, assuming the inner radius to be perfectly accurate, it requires an error of only  $0.03$  mm. in the outer corneal radius to alter the power by  $0.25$  D. A similar error in vertex power would result from making the lens  $0.1$  mm. too thick or too thin.

The thickness of the fluid meniscus is not a negligible factor, since every  $0.1$  mm. of fluid adds approximately  $0.12$  D. to the effective power of the contact lens system. An error in the corneal aperture will affect the thickness of fluid and thus alter the power. For example, an increase of  $0.25$  mm. in the corneal aperture will add about  $+0.12$  D. to the power simply by increasing the fluid thickness. All the above figures are based on average radii and dimensions.

In short, there are several sources of error which may be small in themselves but may quite easily reach a formidable total if their effect is additive. The greatest care should therefore be taken by both manufacturer and prescriber.

One thing which a study of these tolerances has brought home to the author is the extraordinary performance required on the part of nature in order to produce a perfect emmetropic eye.

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OBSERVATIONS ON THE PULSE AND RETINAL  
ARTERIAL PRESSURE

BY

Professor W. KAPUŚCIŃSKI

POZNAN

## Part I—Arterial movements in the pulse

THE investigations into the pulse which I have the intention to make generally known by the present article, are the result of my studies of the problem of measurement of arterial movements in the central retina. Some 30 years ago these measurements were carried out for ophthalmological purposes by P. Bailliar, a French ophthalmologist, who in doing so made use of an instrument specially constructed by him and named by him an ophthalmodynamometer.

Bailliar's method found very wide application, and; in fact, the numbers of publications containing reference to results obtained by it, form to-day a veritable library. This method was the object of an individual theme on the programme of the last Congress of International Oculists in Cairo, 1937. I myself have devoted a good deal of time to this study.

The results of a number of different authors in relation to physiological arterial pressure are not in agreement, the deviation sometimes amounting to 100 per cent. It is therefore not at all surprising that someone has questioned: "What is the cause of this divergence, and is it due either to faulty technique or to an error in the method itself?" Desirous of solving this riddle, I began to inquire into the basis for our knowledge of the arteries. By adopting this procedure, I made reference to observations on the pulse, crystallizing in a separate whole anything relating to problems bearing on this truth. I therefore present in the first part of my article some facts bearing on the subject, although I am, at the same time, fully aware that I enter upon the sphere of the physiologist and specialist of diseases of the internal organs.

Shall I then be able to add something entirely new and nothing but "new facts" unknown to either physiologist or internist, to justify my action? What can I say beyond what physiologists and internists have proved experimentally and clinically as consolidated in text-books on physiology, and completing as such the theory on the pulse?

My reflections on the pulse are due to observations on the fundus oculi arrived at by a procedure on which neither physiologist nor internist has embarked so far.



What does it concern?

In the fundus oculi we see arteries and veins of a kind that we are unable to study from records anywhere. We behold them magnified 14 times.

On examining the fundus oculi, there can be observed the phenomenon of an arterial system, none too distinctly, however, as is often the case, and to this phenomenon little attention has been paid so far, and—it seems to me—that no explanation has ever been attempted.

This phenomenon sets in rhythmic motion the artery branching off from the central retinal artery. It is a movement which is sometimes very distinct, and sometimes most difficult to perceive. In a great many instances it is not perceptible at all.

The movement is to be seen most accurately in the bends of this artery, and the greater the bend, the more distinct becomes the motion.

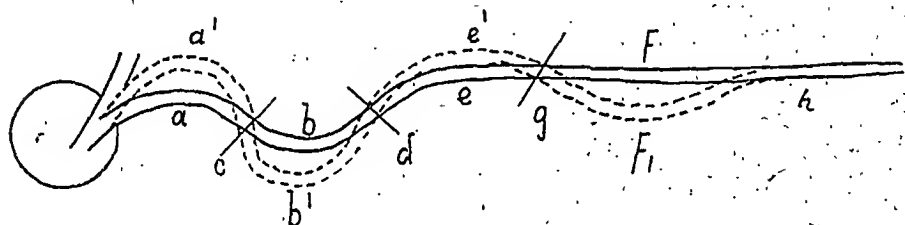


FIG. 1

On the above sketch I have endeavoured to explain this movement. We notice here two prominent peaks of the artery running in an inward direction, *viz.*, the peak *a* and the peak *b*. Simultaneously with the cardiac systole, the peak *a* moves upward to a point *a'* and the peak *b* downwards to a point *b'*. Due to cardiac diastole, the peaks then return to their former positions *a* and *b*. The systolic movement is rapid, whereas the diastolic movement is slower. A diagram would present the following broken line:—

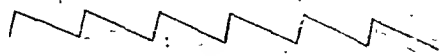


FIG. 2.

This broken line shows the pulse in angular outline, its first phase being rapid, and its second phase slow.

Between the peak *a* and the peak *b* there occurs a small interval where movement is entirely absent, let us call it the point of rest *c*. In the proximity of this point of rest, therefore, the artery performs movements which in the sections *a* and *b* differ from

each other. The smaller the bend of the artery, the shorter will be the rest, but the artery will always indicate two sections representing movements not in harmony with each other in the proximity of the point of rest.

It is very seldom that this rest is to be distinguished immediately on the flowing artery, but even then we are able to distinguish two sections characterized by a different flow near the point of rest in question, and we shall always be able to perceive a rapid systolic phase and a slow diastolic phase. In the proximity of the point of rest, the movement disappears completely.

According to Fig. 1, therefore, this movement takes place through *a* and *b* with the point of rest *c*, then continues through *e* and *f* with the point of rest *g*, and ceases completely when passing on through *h*.

This therefore represents the arterial movement in the fundus oculi in cardiac systole and diastole.

Here it is necessary to emphasize that no other movements are performed by the artery, that is to say, there are no other rhythmic movements in it to record, or, in other words, the artery neither dilates nor contracts.

I wish to point out once more that the movements herein described do not take place *distinctly* in all eyes. Let it suffice to emphasize, however, that they happen very often (in about 80 per cent. of cases), and that they are perceptible only by the application of a certain amount of skill. Their detection is possible when carrying out a series of eye tests for a considerable time in complete absence of movement, which, of course, is not within the reach of everybody. The investigation must only apply to the arch of an inward bent artery. The rhythm of the movements corresponds entirely to the rhythm of the pulse.

This phenomenon was by no means unknown long ago. Attention was paid to the views expressed on circulatory disturbances in Heine's "*Augenuntersuchung bei Allgemeinerkrankungen*" (Gustav Fischer, Jena, 1924). The opinion given therein is, however, quite erroneous, as I will expound later.

Among the literature to which I have had access, I have discovered only one publication by Ballantyne, the British ophthalmologist, who made a remark on the movements referred to above, confirming that they occurred in 36 per cent. of cases of eyes examined.

The nature of such movements had not until then been the object of special investigation.

*In the meantime, the analysis of such movements has had an exceedingly far-reaching significance, due to Bailliart's method and to facts connected with the pulse in general.*

Before proceeding to deal with the factors which are the direct cause of the arterial movement in the pulse, I am anxious to take into consideration the question bearing on my own observation, namely, *whether the arterial movements noticed in the eye are peculiar only to the central retinal artery, or whether this phenomenon can also occur in other visible arteries.*

In addition to the arteries of the fundus oculi, there are not many visible arteries. They are not seen *directly* as in the eye, but *indirectly* through the skin.

Under different circumstances, and in different places, arteries become visible in people. An artery, for instance, is ramified very differently in old persons of the emaciated and of the flabby type with high blood pressure. Thus the pulse of such an artery in the vicinity of the elbow joint, due to the running of collateral arteries, appears to be very different. They flow at a depth of 1 cm. or more under the skin.

We therefore observe the same movement as in the artery of the fundus oculi. But even in the other arteries we are able to perceive the pulse. In my personal self, for instance, these movements appear in the extension of the radial artery between the thumb and the index finger on the inner side of the left hand in its inward flow. It is also to be perceived by slight pressure with the palm on the ulnar artery in suitable illumination. These movements also appear in the temporal artery and in the dorsalis pedis. Further, it is seen in the femoral artery under Poupart's ligament. A certain amount of practice is required in order to be able to see it. Undoubtedly, there occur movements in the whole arterial system. *These movements are nothing else than the pulse.* This pulse, however, as it is felt in the radial artery, we interpret as rhythmic rising and falling of the arterial wall. This interpretation is erroneous, because it is obvious that the artery does not undergo expansion even to the extent of a fraction of a millimetre. The cause of this erroneous interpretation is the fact that the said artery runs in a groove between an offshoot of the radius and muscular tendons.

In this groove the artery can only perform its upward movement, and, therefore, the movement in question at the side of the finger—taken as an example—is such that we receive an erroneous sensation of the rhythmic dilatation and contraction of the artery. In all arteries where we feel the pulse, it is nothing but an arterial pressure movement and by no means dilatation of the arterial tube; *the arterial tube in cardiac systole and diastole remains unchanged.*

*The above results in regard to the arterial movements are based on indubitable facts. These facts do not require any further discussion.*

From these facts it is now necessary to draw adequate conclusions. Before proceeding with this, I will answer the question which is bound to suggest itself to everybody, namely: Are the above mentioned remarks known in literature, or has nothing so far been written on such obvious phenomena? It is here necessary to establish whether these facts are fully mentioned in text-books on Physiology. Neither in Beck's manual, nor in Tigerstedt's, nor Höber's (1930), nor Rein's latest edition (1943), nor Landois-Rosemann's (1944), nor Tigerstedt's fundamental 3-volume work on the revolutions in physiology, is there the least mention of these phenomena. Only in Beth's 1925 text-book ("Handbuch der normalen und pathologischen Physiologie," Julius Springer, Berlin), comprising about a dozen volumes, we meet in Vol. 7 in the section on the Arterial and Capillary Pulse by Frey on p. 1224 with the following remark: "... what we find in regard to the pulse is a change, as it were, in the position rather than in the volume of the artery during pulsation ..."

From this observation the author did not, however, draw any conclusion, because he did not fully estimate the importance of the phenomenon, and he contented himself only with the above cursory, suggestive remark. However little this writer, in fact, commented on this observation, there is a further remark in connection with his deductions on p. 1238, where he states: "under normal conditions this *vascular dilatation*\* at the time of cardiac systole is the measurement of the increase of pressure."

Thus the author reverts once more to the conception of vascular dilatation in systole.

Apart from the above brief remark, we cannot find any further reference to arterial pressure movements in text-books on physiology.

As regards French and English text-books, I have not been in the position of availing myself of these.

This negative evidence, however, did not satisfy me, for the very reason that it was hard to believe that the state of things described by me had altogether escaped the notice of scientists. I therefore set about my research work to find out the actual position of the question. To start with, this was a difficult task under the present circumstances. Thanks to the kindness of the junior colleagues of Dr. A. Horst, I came across a book published by G. Hauffe in 1930 on the cardiac pulse and circulation (Lehmanns-Verlag, Munich). It is a book in which the author struggles with his huge original treatises on the heart, blood stream, electrocardiogram, pulse, etc. The greater part of Hauffe's works is of interest outside my own sphere. In his

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\* The italics are mine.

observation, however, on arterial movements as described by me, he is in agreement on almost every point.

Moreover, Hauffe quotes earlier literature in which occur descriptions of the very same ideas. He quotes Volkmann who, as far back as 1850, wrote as follows: "If we lay bare an artery, we shall find that it assumes a tortuous position, and that it afterwards returns to a straight position" and "... measured by compasses, the arteries do not show a tendency to dilatation at the time of the pulse." Volkmann further cites Rudolphi, the predecessor of Johannes Müller in the Chair of Physiology in Berlin. Rudolphi proves that the arteries at the time of the pulse do not dilate. Hauffe also quotes Mackenzie who in 1904 wrote as follows: "What we perceive as a movement of the pulse, upsets our notion completely. By investigating this more closely, we shall find that the artery changes its position. A pulsating artery never undergoes a change in volume, but changes its position. The opinion that the pulse depends on the dilation of the blood vessel in question, or that it is due to the "throbbing" of its wall, is erroneous." I am quoting these authors according to Hauffe, but have had no opportunity of reading their works in the original. However, not a single one among these authors has offered any further suggestions with regard to the mechanism of the pulse on the basis of their observations.

Hauffe himself barely does it, and yet—all his arguments are not convincing. For example, Hauffe maintains that only the pulsating artery in the proximity of the place of pulsation assumes a curved course, either artificially or physiologically. This assertion is not quite correct. The arterial winding is unnecessary for giving rise to these movements, but the conclusive point is that the circulatory system be closed. In the arteries of the fundus oculi there occur no windings in spite of the pulse. This pulse has been the object of my present deductions. Thus Hauffe is unaware of anything concerning the arterial pulse of the fundus oculi.

Anyhow, after passing a review of the value of Hauffe's work, we have no doubt that he has expressed an adequate remark on exactly the phenomenon described by myself, though, of course, he has not drawn any serviceable conclusions at all from his observation.

I will now revert to the discussion of the true significance of the problem, namely, in relation to Bailliart's method. The question arises whether Bailliart arrives at the conclusion that there are indications of arterial movements in the pulse or, as the case may be, of any factors to which these movements are due.

As I have stated on the strength of my observations, movements

appear simultaneously with the cardiac systole and diastole. There can be no doubt whatsoever as to their being dependent on systole and diastole. Simultaneously with the systole, there results an arterial movement, and due to diastole the artery returns to its former position. As systole and diastole are factors prompting changes in pressure in the blood stream, the visible arterial movements are also exponents of such changes in pressure. If in systole and diastole the blood pressure remained unchanged (as maintained by Hauffe), these movements would not be due to this. The pressure would remain unchanged, if the arterial system remained an open system. (There would then occur changes in kinetic energy in systole and diastole, and also changes in the rapidity of the flow of the blood stream.) Turning it round the other way, the greater the difference between systolic and diastolic pressure, the more prominent would be the pressure movements.

We are, indeed, able to observe these changes in the fundus oculi. As I have already previously pointed out, these movements are hardly perceptible under normal conditions, and are often altogether invisible. On the other hand, in cases of rapid pulse, where the difference between systolic and diastolic pressure is known, for example, where it reaches 100, the arterial movements in the fundus oculi are very distinct, being visible without difficulty even to the naked eye. The conclusions mentioned a little while ago would immediately suggest to us that a difference between arterial systole and diastole of 0.1 mm. (arteries in the fundus oculi) is the minimum under normal conditions. This assertion is of immense importance for the estimation of Bailliar's method, but I do not now wish to dwell on it, and will therefore leave these arguments for a later part of my article.

In fact, I might as well deal with the pulse, as, after all, my present conclusions afford me a basis on which to develop my criticism of Bailliar's method. It is my intention, however, to solve the problem of the pulse as raised by me and to present it as a synthetic whole. I am of opinion that by doing so I shall be able to fill a certain gap in the theory of the pulse.

With this task in front of me, I must proceed from certain fundamental facts to arrive at a basis for my arguments.

I will try, first of all, to give an explanation of the origin of the arterial pressure movements, which gave rise to my inquiry. The proof that these movements have their origin in direct dependence on systolic and diastolic pressure does not yet explain the *mechanism* of the origin of these movements. To explain this mechanism, we must first confirm the fact that the circulation of the blood takes place in a closed system. As a matter of fact, any area of capillary vessels is several times larger than the aortic

area; this, however, the blood stream encounters in proportion as it passes into circulation, causing, when resistance is offered, a compression of the blood vessels and, above all, an increase of the viscosity of the blood. This kind of resistance determines the fact that the blood stream must be regarded as a closed system. At the same time, due to the cardiac systole, the blood receives the given impetus. This impetus produces an increase of pressure, which, according to Pascal's law, is distributed simultaneously throughout the arterial system. An impetus, taking the place of the "arterial bend," prompts arterial movement in the direction in which it works. The impetus makes itself strongly felt at the beginning of the circulation of blood, but, due to a number of factors, such as vascular contraction, viscosity of the blood, etc., this impetus weakens, and the kinetic energy changes into thermal energy. For the very same reason, the arterial movements also gradually decline in extent. In my opinion, this may also conveniently represent the mechanism of the arterial movements in the pulse.

As quoted by me, Hauffe compared the movement of the arterial system with the folding of a taut string. Such a comparison is not quite adequate, as in the case of the folding of the string both phases are equal. In fact, as I have already emphasized repeatedly, the phases are unequal, one being rapid and the other slow, a circumstance known to us from the pulse curve.

However, the problem of the pulse is not exhausted by the interpretation of the mechanism of resistance in arterial movements. This proof is of particular significance for investigations into retinal arterial pressure, but cover only a small section of the entire problem of the pulse.

*The presence of arterial pressure movements as well as the lack of any traces of contraction and dilatation of the arteries in the pulse serve to establish facts which are in no way compatible with the present position of the theory on the pulse.*

Allow me to enumerate the factors which, according to the present theories of the physiologists on the mechanism of the blood stream, contribute in playing a rôle.

The main factor is the cardiac muscle, acting as a compressing and suction pump. The assistant factors are the arteries. The work of the arteries, as already stated, is accomplished—according to the description in all text-books by physiologists—as follows: The cardiac systole causes the blood wave to be thrust onward to the artery, and dilates it in a certain limited section; in the next phase, due to the action of the muscle, the artery contracts. This arterial movement takes place throughout the

arterial system, giving rise to the same kind of peristalsis. Due to this arterial movement, therefore, there is, on the one hand, a perceptible pulse and, on the other hand, peristaltic movements serving the purpose of a powerful factor in setting the blood stream in circulation.

In contrast to this theory, we have in Beth's treatise the views on vascular peristalsis.

In the chapter on the auxiliary function of the blood vessels in the circulation on p. 1071, its author, Alfred Fleisch, while basing himself on his own evidence and that of Hürthl, arrives at the conclusion that arterial peristalsis does not exist. To quote his own words, Fleisch writes on p. 1083 as follows: "... by this assertion it is confirmed that neither large nor small arteries perform any systolic movements. The arteries are provided with the very same tubes, but do not produce any active force to set the blood stream in motion." Fleisch also denies the existence of a so-called "cardiac circulation" having its say in the peristalsis of capillary vessels. It need not be emphasized that Fleisch's views in their essence are in accordance with my observations.\*

These deductions on the part of Fleisch have not found their way to text-books on physiology, so that the views expressed in the foregoing still prevail in the science of to-day.

The theory on the pulse denies the facts suggested by me: the pulsating artery (with the exception, perhaps, of the commencement of the aorta) neither dilates nor effects a peristaltic movement.

Let us, however, attempt once more to consider critically this theory on the pulse dominating as it does all text-books on physiology. According to this theory, the work of the cardiac muscle would not be made use of in the onward motion of the blood stream in the circulation, but a certain part of this force would be used in surmounting the resistance of the vascular muscle and this, in fact, simultaneously throughout the arterial system. This simultaneous dilatation of the arterial tubes of the whole circulatory system would necessarily cause reduced pressure in the whole system.

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\* With regard to the theory on the pulse expounded in the above mentioned text-book, one cannot help noticing that there exists an appreciable divergence of opinion which, I venture to say, leads to utter confusion. Two authors, Frey and Fleisch, have worked on the same subject, advancing views that are altogether different. Undoubtedly, Fleisch arrives nearer the truth, though even he comes to a standstill, as it were, in the pursuit of his investigations. He contents himself by denying the co-operation of the vessels in the onward thrust of the blood stream. This denial is based on the lack of peristalsis in the artery. However, the opinion of Fleisch is only partly correct. The lack of peristaltic movements does not so far prove that the artery has an active share in the onward thrust of the blood stream. A little further on, however, he states that the arteries prove to be in apparent co-operation in the onward thrust of the blood stream, though they do not perform peristaltic movements.



As regards the following (false) arterial systole which would level out the pressure, and would thrust the blood onward in circulation, it is obvious that this could happen only if the systole is peristaltic, as, indeed, taught by the physiologists, but there has been no one hitherto able to prove it.

The *cardiac* systole would correspond to the *arterial* diastole and, *vice versa*, the cardiac diastole to the arterial systole. When examining blood pressure, we distinguish between systolic and diastolic pressure. Systolic pressure we should still describe, in accordance with the views held up to now, as the phenomenon when the artery dilates due to cardiac systole, and diastolic pressure when it contracts.

In consideration of this, it follows that systolic pressure at the time of arterial dilatation must be lower than diastolic pressure at the time of contraction. This is obviously inadmissible, but according to the present views on the rise of the pulse, I do not see any possibility of grasping this matter otherwise. It is necessary also to remember that a hardened artery, sometimes hard as lead, pulsates more rapidly than a soft artery, and it pulsates not because of dilatation of its tube, but due to a pressure movement affecting the whole artery to be felt by our testing finger.

Thus we shall find that the theory hitherto on the pulse and the circulation of the blood cannot be criticized merely on the ground of this theoretical consideration. Yet, basing ourselves on arterial pressure movements, and in consideration of the non-occurrence of any apparent contractions or dilatations of the arteries, it proves absolutely untenable.

Further, it is necessary to prove that the third factor which, according to the text-books of physiologists, is an auxiliary force in the blood stream, in the sense given by physiologists does not exist. Such being the case, the question arises why the two factors connected with the cardiac action resembling a compressing and suction pump, are not sufficient for the blood stream.

Now we have also to prove that if the blood stream were dependent only on these two factors, it would not reach the perfection which indeed it does.

The German surgeon Bier expressed the following opinion: When performing the amputation of a foot, there arises the question of Esmarch's bandage. As soon as the amputation has been carried out, it is necessary to cover up carefully all arteries before the removal of the bandage in order to prevent haemorrhage. In cases of hardening of the arteries the bandage may be removed before tying up the vessels, and no blood from hardened vessels will flow out. I quote this statement on the responsibility of Hauffe, who, however, does not refer to it in his book.

What does this statement imply?

It simply implies that in non-hardened arteries the third factor, the motorial, operates where the second factor, the suctorial, is eliminated at the resection of the vessels. In hardened arteries, however, it does not function. The question also arises how the third factor is functioning and whether it is functioning in the way described in the text-books. In order to comprehend the working of that factor, let us realize its general significance from what is known from physics. The basis for the experiment selected is a row of elastic balls suspended on cords. The balls are placed so that they touch each other. We lift up the first ball, thereby giving it potential energy. We then let go this ball, so that it touches the remaining row of balls, when the last ball in the row rebounds from the rest and the others remain motionless. What do we witness here? The potential energy given to the first ball changes into kinetic energy during the lowering of that ball. This kinetic energy at the striking of the remaining balls changes into potential energy, which once more becomes kinetic energy in relation to the last ball when moved from its place.

The same thing takes place in the blood circulation, *viz.*: potential energy created by the systole of the cardiac muscle is transferred to a section of the artery as kinetic energy, thereby effecting arterial movement. At the same time, a part of that energy continues as potential energy at the wall of the artery, which immediately restores it to diastole in the form of kinetic energy of the blood stream. In the event of the vascular walls being hardened, the change of potential into kinetic energy becomes much reduced, owing to the third factor losing its force of action in a large measure. Such being the case—as already quoted by me from the text-book—the potential energy given to the blood by the heart diminishes gradually to a limit varying due to the effect of several factors connected with calorific energy, and, as a result of its centrifugal action, it does not hamper the circulation of the blood, but is in harmony with it.

As quoted by me above, Hauffe likewise attempts to explain the task of the third factor.

Thus Hauffe refers to the rubber tube test cited by him on a previous occasion. In physics this test is known as "Bernouille's test."

He bases his explanation on the following observation: If we admit through an open rubber tube a stream of water, the swifter the current of water, the tighter will become the tube. The same phenomenon can be seen on an X-Ray screen in the aorta. Hauffe proves that the artery contracts due to cardiac systole, and that

diastole causes it to dilate. Simultaneously with the dilatation there appears tension in the arterial wall, by way of potential energy, which at the following systolic movement is converted into kinetic energy assisting the onflow of the blood stream.

Hauffe was not aware of the publication of Bronislaw Sabat's article in the Lwow Medical Compendium in 1911. In this article Sabat describes the radiokinographical method employed by him, which he applied to all organs performing movements. By the aid of this method he was able to prove that the aorta, above all, performs pressure movements. Bernouille's phenomenon of the aorta does not arrive nearer the truth.\*

I therefore think that the third factor, the acceptance of which seems indispensable, is performing its work in the way demonstrated by me.

In connection with the actual behaviour of the mechanism of the blood stream, there arises a series of problems† the mention of which would exceed the limits of my task, the more so as some of them would require experiments which under the present circumstances I am unable to carry out. Nevertheless, I should like to dwell on two problems connected with theories developed by me, although they happen to be outside the scope of my present subject.

I wish to bring further light on some remarks on the pulse. Above all, it is my desire to make it known once and for all that I have no intention to review the whole of this problem. In consideration of the immense work and the numerous experiments devoted on this problem, a full account would necessitate a separate monograph. Moreover, in order to give conclusive evidence in such a problem, it would be necessary to do so, in the first place, by way of proofs which, as stated above, I am unable to produce. I only intend to make a few remarks which—it would seem to me—have a bearing on my previous deductions.

As quoted by me above in a number of instances, Hauffe proves that the pulse is an artificial phenomenon due to arterial pressure. In my opinion, Hauffe's proof is unquestionably correct. In the absence of arterial pressure, the pulse curve would necessarily describe a different course, *i.e.*, the curve would not develop

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\* A description of the same method was published on the appearance of Sabat's article by Gött and Rosenthal. In a monograph on kinography Prof. Pleikart Stumpf makes mention of Sabat as the first to give a description of the radiokinographic method. After the appearance of Sabat's article, my attention was called, among others, to Prof. K. Mayer's remarks, for which I tender my heartiest thanks.

† In the physiology of the text-books there is quoted the rubber tube test by way of an example of the circulatory conditions and the appearance of the waves. In the rubber tube one is able to reproduce the peristaltic wave movement and to finish it off with the rebounding effect in question. On this comparison depends the unfortunate misunderstanding which led to the distortion of the theory on the pulse. However, a rubber tube device can be identified with an artery only with due reserve.

capriciously due to pressure, but would necessarily reflect any movement emanating from the artery. What the curve would look like then, I cannot tell. I do not think the completion of such evidence under favourable circumstances would be a difficult matter. Unfortunately, it is not possible for me to do so. It would be of uncommon interest, were it proved that such a curve appears also in a dicrotic phase.

As regards this dicrotic phase in the pressure pulse, it is difficult to become reconciled with even the best of theories. This phase must necessarily be simultaneous with the rebounding of the pulse wave from the capillary area. Such a theory, however, is not altogether acceptable. The pulse wave, for the reason that it fades out in the area in question, changes—as I have already mentioned in the foregoing—into thermal energy. Moreover, the pulse wave proceeding from the cardiac valve, cannot change, but—as we have proved—must flow onwards, and not backwards. Such a wave could reverse its course only in the event of a standstill of the blood pillar, but could not run against the current in the wrong direction.

Whence, therefore, does the dicrotic phase arise, and what is the origin of occasional protuberances that may occur?

Hauffe conjectures that they are an expression of the throbbing of the entire arterial system, a throbbing which continues from the first impetus due to the cardiac muscle systole. He compares this throbbing to the vibration of a taut string.

It is necessary to remember that the pulse wave can manifest itself only in the arterial walls. It then manifests itself as an arterial pressure movement produced by changes in the pressure of the blood stream; inside the artery in the vicinity of the arterial walls enclosing the liquid the blood stream indicates changes in pressure only periodically. A manometric test shows a curve corresponding to the pulse curve, because it also covers the dicrotic phase and other vibrations. In this curve obtained manometrically, as well as in the pulse curve, the continued vibrations cannot be produced by a return wave.

How is it possible to conjecture such a thing as that the blood stream should arrive at a complete standstill, as asserted by Franke, in order to flow back to the heart?

Is it possible to show a greater waste of energy of the heart, should this theory prove to be the true state of things? The heart has to spend its energy on the dilatation of the vascular tubes of the entire arterial system, and afterwards indirectly, due to peristaltic contraction of the dilated artery, has to serve the purpose of a permanent blood pillar impelled to supply the circulation. Instead of profiting by the existing blood stream, the

cardiac force and, indirectly, the arteries, must 72 times a minute move on the blood arriving at a standstill. Is it possible that some motor power or other disposes of that energy so uneconomically?

The blood stream cannot arrive at a standstill. From the first phase in the genesis of its existence when the blood serum is collected from the circulation in a cardiac tube, the heart is through this tube in direct communication with the arterial system. From this moment, the onflow of the blood stream continues uninterruptedly, receiving a constant rhythmic stimulus due to the cardiac systole. Thus it happens that an inert force is stirred to life, commencing with the first cardiac systole until death, and until the heart stops beating; the blood stream on death no longer receives an impetus, as there is no outflow from the arterial system, the arteries being left empty, at death.

This brings my reflections on the pulse to an end, and I will now give the following brief summary. In the fundus oculi we observe simultaneously with the pulse, arterial movements depending on the impetus given by the local artery. These movements appear in two phases. The first phase, due to cardiac systole, is rapid, the second, due to diastole, slow. Any other movements, viz., arterial dilatation and contraction; do not take place. We observe the same pressure movements in all arteries of visible organisms, and there are no other movements performed by the arteries. The pressure movements in question are directly due to cardiac systole and diastole, and arise as the result of periodical changes in arterial pressure. Notwithstanding that the arteries do not perform peristaltic movements, they are, thanks to their structure, able to give an impetus to the onflow of the blood stream in the circulation on the basis of simple mechanical laws. The arterial pressure movements are actually the pulse. The pulse therefore does not depend on arterial dilatation and contraction. The above mentioned facts about arterial pressure movements together with the complete immobility of the arterial tubes, lead to the conviction of the unreality of the present theory on the cause of the pulse. A "false" pulse is met with in the artificial product caused by pressure. The blood stream in its first phase originates at the genesis of life, and continues to flow on uninterruptedly, receiving a rhythmic stimulus due to cardiac systole.

## Part II—Measurement of pressure in the retinal artery system

I will now pass on to the discussion of Bailliar's method, and wish once more to emphasize the very great practical and theoretical significance to be ascribed to this method. In support of this

test there arose a number of theories, such as the theory of the rise of choked disk or papilloedema, pseudoneuritis of the optic nerve, and atrophy of the optic nerve in tabes dorsalis (locomotor ataxia) and in glaucoma (Sobanski, Lauber).

Various other optical disturbances and retinal troubles due to vascular disturbances, have been revealed, as it were, by means of the ophthalmodynamometer. The extent of interest attached to Bailliant's method in the ophthalmological world has of late years diminished considerably. As far as Schiötz's tonometer is concerned, it supplied an indispensable need in connection with the question of ocular instruments in cases where Bailliant's ophthalmodynamometer very often proved useless, as generally happens in the hands of practitioners.

It would seem accurate to say that the significance of the ophthalmodynamometer should in no way be regarded as less than that of the tonometer. The study of the conditions of the circulation of the blood in the retina must have a significance equal to the examination of blood pressure in the arterial ramification and, maybe, even surpass it in importance. The present investigation, however, claims the possibility of estimation not only of arterial pressure, but also of the main conditions in the venous system, resulting from the material relations of both systems, and also in relation to general blood pressure and internal pressure.

Such claims on the part of Bailliant's method are outside its scope, or come into consideration only on a very limited scale.

The most appropriate reproach which can be made against this method is the divergence of the results obtained thereby. The divergence is here very great indeed. I permit myself to quote the results of some authors in regard to arterial pressure:—

	Diatolic pressure.	Systolic pressure	
Sobanski .. ..	48 — 56	80 — 90	
Bailliant ....	30 — 35	65 — 70	
Duverger Barre ...	50 — 60	80 — 100	
Samoilow ... ..	35 —	80 — 85	
Magitot and Bailliant (in the dog)	50 — 65	80 — 90	
Blidung ... ..	70 —	117	

Quoted from Weiss's "Kurzes Handbuch für Ophthalmologie."

This divergence was lately emphasized by Behr ("*Zentralblatt für gemeine Ophthalmologie*," p. 70). I do not intend to repeat these deductions, but would refer the reader to the article in question.

There are, however, other sides of the problem that are of paramount interest to me, and I am anxious to find out whether the divergence of the above-mentioned deductions depends on the technique employed in the investigations, or whether it is also due to the method itself. I should like to speak critically of the soundness of the basis of the whole method as such, and it is possible that the basis of this method must be questioned, and that therein is to be sought the fundamental error which is the cause of the deviations of the results arrived at (and, at the same time, their contradiction to established facts). The method of investigation of retinal arterial pressure, in fact, is borrowed from the method employed in the determination of pressure in an arterial ramification. In consideration that the method of investigation of pressure in an arterial ramification does not call for any fundamental reservations of being of direct advantage to the method itself and of ensuring exactness as to results, we will examine, one by one, the factors presented to us in the course of this evidence.

We apply on the forearm a bandage which must be sufficiently wide. By this bandage we exercise indirect pressure on the brachial artery. The amount of this pressure we measure by means of a suitable instrument. The factor is the pulse in the radial or ulnar artery. The moment when the pulse begins to decline is chosen for the measurement of diastolic pressure, and the moment when the pulse becomes incapable of being felt for that of systolic pressure.

What is then the method of measuring retinal arterial pressure according to Bailliart? First of all, as necessarily appertaining to the technique of the method, we examine the pressure in the brachial artery: Thus, in the first place, the artery must contract, as a fundamental condition, on a wide distance in the front of the eyeball and, at all events, in front of its ramification in the vascular funnel; secondly, the factor must be the pulse in one of the ramifications of the central artery, that is to say, the *spontaneous* pulse as met with in the above-mentioned artery. This is the way, therefore, the experiment has to be carried out to serve the purpose of an adequate method of measuring blood pressure in arterioles. We will now examine what actually happens when applying Bailliart's method to measurements of central retinal arterial pressure. Here, likewise, we exert indirect pressure on the artery, but not on the artery in the vascular funnel together with its ramifications. We

observe then the so-called arterial pulse. This "arterial pulse" depends on the following phenomenon: In connection with the pressure on the eyeball at any given moment we perceive rhythmic arterial contraction and, as the case may be, dilatation. The resulting arterial movement served Bailliant as a factor for determining arterial diastolic pressure in the central retina, and, on the other hand, as a factor for arterial systolic pressure, the decline of that movement at increased pressure on the eyeball. *The rhythmic arterial contraction and, as the case may be, dilatation of the central retinal artery is generally known to ophthalmologists as a spontaneous arterial pulse.* It is exactly in this restraining procedure that the first error of Bailliant's method is involved.

Thus this method was adopted on the suggestion of the view held hitherto on the essence of the pulse, it being believed that it depends on the rhythmic dilatation and contraction of the arterial tube. A similar phenomenon was noticed in the retinal artery, and these movements were regarded as sufficient to determine the pulse. The suggestion afforded by the theory held so far on the pulse was altogether too great, and yet, it had not even been ascertained whether the rhythm of the movements in the central artery is altogether different from that of the pulse. The theory on the pulse sets forth that due to cardiac systole there appears, first of all, arterial dilatation, and due to diastole-arterial contraction. The dilatation is a rapid phase, but the contraction a slow one. With reference to pressure "pulse," it is not ascertained whether the phases in the retinal artery happen in inverted order, so that, first of all, due to cardiac systole, there is a rapid phase expressing itself by way of *contraction*, followed by a slow phase, due to diastole, indicated by *dilatation*. The origin of this "false" pulse and of slow factors I will discuss in detail in the following.

For the present, I would emphasize that there is no analogy between the method of examining pressure in an arterial ramification and that used in determining pressure in a central retinal artery, there being only an apparent resemblance, due to a similarity of mechanism. When taking into consideration all the above-mentioned facts, it is necessary to prove that the difference between these two methods of determining pressure depends on the following points:—

*First*, on the change in pressure exerted directly on the eyeball, i.e., the organ in which arterial pressure has to be investigated.

*Secondly*, on the completely changed factor, because the "pulse," which we regard as the factor, has nothing in common with the spontaneous pulse due to pressure. To the spontaneous



pulse described in Part I of this article, attention has not been paid in full.

*Thirdly*, on the evidence of completely changed conditions in the organ examined, which are discovered when the examination is carried out under increased pressure.

It is, however, possible that these variations in the method of investigation are no fundamental errors, and that this method does not lead to false results. In other words, it may be questioned why, despite the changed conditions in the way of carrying out the examination, the results of Bailliar's method, nevertheless, do not give us an insight into the true conditions of pressure in the retinal arterial system.

Let us endeavour to examine this problem from its purely theoretical standpoint. According to Bailliar's method, the proportion between systolic and diastolic arterial pressure equals 0.45:1. However, such an estimate cannot be absolutely in correspondence with the true state of things. Due to the circumstance that in the retinal arteries the spontaneous pulse is not altogether apparent, but, in the majority of cases, a hardly perceptible or an entirely imperceptible feature, the difference, therefore, between systolic and diastolic pressure must be very much less. The reason for this assumption is that the pulse movements, as shown in Part I of this article, are dependent, above all, on the difference between systolic and diastolic pressure. If the relation between systolic and diastolic pressure was, in fact, equal to 0.45:1, then the margin would exceed that in the brachial artery, where the proportion is, more or less, 0.6:1.\*

The physiological pulse in the retinal arteries should therefore be quite perceptible in every eye, and should even be more distinct than in the above-mentioned artery.

In consideration of the fact that, as already mentioned, the physiological pulse is much lower than would even appear to be the case, we must conclude that in the central retinal artery the difference between systolic and diastolic pressure is inappreciable. In diseases of the arterial system, in valvular trouble or, in general, in cases of rapid pulse, it is bound to be very much more distinct

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\* The manometric test made by Duke-Elder on cats, gave the following results: in the central artery 59/69 to 83/94; in the ophthalmic artery 53/85 to 108/129, corresponding to the proportion of 0.7:1 in the central artery, and the proportion of 0.5:1 or 0.66:1 in the ophthalmic artery. The difference therefore in the central artery between diastolic and systolic pressure is less than the difference shown by Bailliar's method (0.45:1). However, Duke-Elder's method depending as it does on the aperture due to inserting a glass tube into the arterial tube, must necessarily show this reduced value. It would, nevertheless, be necessary to prove that this method, the subtle technique of which must be admired, does not change the conditions of arterial pressure.

than in cases of natural flow of the blood stream, as already mentioned in Part I of my article. The foregoing theoretical considerations therefore lead to the suggestion that here occurs a fundamental error, due to Bailliar's method. There also occur other shortcomings, for example, the maximum pressure indicated by Bailliar's method is doubtful. The maximum systolic pressure amounts to—more or less—80 mm. Hg.

In view of the fact that the pressure in a vein must amount to, more or less, 20 mm. Hg, it would have to be proved that this great decrease in pressure occurring within the eyeball along a distance of 4 cm., can also be considerably less. The maximum reduction in pressure occurs in the arterioles. The maximum resistance in the circulation of the blood is created in the arterioles and capillary vessels, but physiology does not provide us with any accurate measurements. We are, however, able to assume that in the retinal arteries which count with fractions of a millimetre, the pressure is bound to be reduced considerably (as regards the pressure in capillary vessels to the extent of at least one-eleventh of the general blood pressure). We shall also find that the velocity of the blood stream in capillary vessels is exceedingly small, amounting to no more than a fraction of a millimetre per second. The interpretation of the appropriateness of this spontaneous flow is probably superfluous. For the maintenance of this spontaneous flow, the assumption must be made of a gentle and by no means sudden reduction in pressure. Moreover, one is bound to be struck by the non-correspondence of the reduction in pressure from the large blood vessels to the central retinal artery :  $130 - 80$  equals 50, and from the said artery to the vein :  $80 - 20$  equals 60. The above-mentioned theoretical considerations agree with results based on the true facts connected with the physiological pulse, thereby emphasizing further the fundamental error of Bailliar's method.

For the further elucidation of this interesting problem we will in the following deal with the origin of the "pressure pulse."

It is a most significant fact that ever since the dawn of the era of investigation, that is to say, for nearly a century, inquiries have been made into the origin of the venous pulse, and even to-day debates continue on that question. On the other hand, the manifestations of "pulsation" in the arteries are not heeded at present, and the interpretation given 90 years ago, as formulated by A. v. Graefe, is still accepted.

As a matter of fact, v. Graefe proves that at a moment when due to pressure on the eyeball the pressure within the eyeball is higher than the diastolic pressure of the central artery, the artery at that very moment must begin to pulsate, and, provided only that the

flow is accompanied by pulse waves, the arterial pressure will remain sufficiently high to enable blood to be pumped into the inner section of the artery.

Before making a critical investigation of the arterial "pulse" in the eyeball, we have to examine in brief the problem of the venous "pulse." It will not be necessary to mention in detail all theories expounded on this subject. Reference is only made to Serre's article in the *Arch. f. Ophthalm.*, 1937, in which the author established the passivity of the venous pulse on the basis of cinematograph films, and it is impossible that it could be otherwise. The ocular veins cannot but "pulsate" passively. The type of arterial fluctuating pressure is experienced in the large veins in the vicinity of the heart, where the pressure is negative and where fluctuating pressure occurs (vestibule of vena cava). In the veins of the circulation the blood stream is uniformly without any fluctuation in the pressure. The retinal veins are by no means an exception. It is therefore out of the question that, as suggested by Türk and, in the main outlines, by Sobanski, the venous pulse is a spontaneous "pulse" caused by the transfer of the arterial pulse by way of capillary blood vessels to the veins. This pulse, however—I repeat this fact once more—is apt to decline in surroundings where the potential energy is transformed into caloric energy. It cannot therefore be denied that the arterial pulse is transferred by means of capillary vessels to the veins.

There cannot be any doubt whatsoever that the "pulsation" in the veins is a passive type of "pulsation" produced by fluctuating interior pressure. Simultaneously with cardiac systole there is propagated to the eyeball a wave of blood, which engages in rhythmic fluctuating interior ocular pressure. No other force can here come into consideration. The venous blood-pressure equals the lower pressure in the interior of the eyeball. It can be higher—even considerably higher—but can never be lower than the latter. *We can measure this pressure by Bailliant's method.* In this connection, I should like to point out from what has been stated above that by Bailliant's whole test method only in the investigation of venous blood-pressure do we arrive at results which are, more or less, in accordance with the true state of affairs, but one thing is quite clear, and that is that this method is not serviceable in measuring systolic and diastolic venous blood-pressure, for, as I have pointed out in the foregoing, such a difference does not exist at all. The possibility of an accurate definition of pressure seldom presents itself, and this for the following reasons: the height of pressure would correspond to the pressure force necessary for the production of the first palpitation of the pulse in the funnel-shaped

vein in the depth of the disc of the optic nerve, in the distant part of the vein where the pressure in that vein must be the lowest.

Has therefore the first palpitation of the "false" pulse that signification? A straightforward answer is: a pressure force able to exercise even a little pressure on the venous wall must exceed the pressure in that vein. This ideal equilibrium between the pressure in the vein and the impetus of pressure is not possible to be determined by the aid of any factor; it is therefore necessary to load the frame, as it were, by a trifle more weight to incline a little to one side in order to produce the first artificial movement of pulsation, that is to say, by giving way to the venous tube. For the purpose of accuracy of the result read on the Bailliant scale it would be necessary to add the pressure exerted by the increased tension of the eyeball due to cardiac systole, and also the forces causing the first throb of pulsation in the vein. These forces can be calculated from the rhythmic beats recorded by a Schiötz's tonometer, which amounts to, more or less, 2 mm. Hg to 3 mm. Hg. However, all instruments do not indicate the systolic throb in eyeball pressure. In this way, the above-mentioned investigation gives us results which are unquestionably a trifle too high as regards venous blood-pressure, but, in my opinion, the error is not very great.

When measuring venous blood-pressure in the eyeball where spontaneous "venous pulsation" exists, it will be necessary, first of all, to lower the pressure in the eyeball, which, as we shall find, is not a difficult matter. Measurements, however, on a soaked eyeball cannot, for obvious reasons, be accurate.

There is no doubt that the only measurements that possess a value are carried out on an eyeball having lower pressure than the venous blood-pressure or, expressed otherwise, where the venous blood-pressure is much higher than the pressure in the eyeball. Above all, the application of Bailliant's method can give positive results in cases of inflammation of the ocular nerve and of choked disc (papilloedema), due to increased central pressure.

That the venous blood-pressure is in a fixed relation to the central pressure, and that it is possible in each case to calculate the central pressure from the venous blood-pressure, as proved by Baumann and Sobanski, about which, however, I find it difficult to express my opinion, and I will therefore abstain from dealing with these problems. Such rigid relations between the eye and the brain, that is to say, between venous blood-pressure and pressure on the cerebro-spinal canal would, I think, be rather unlikely to meet in a living organism.

Summing up the above results, it would be necessary to prove as follows: The "false" venous pulsation in the retina is always

passive, apart from what is due to interior pressure and cases when the pressure is "spontaneous." The extreme cause is always a rhythmic palpitation due to central eyeball pressure. The blood wave in the vein is uniform, the blood stream even and without palpitation due to pressure, and it is not therefore possible to ascertain the difference between systolic and diastolic pressure. Instead of this, it is possible to measure by Bailliart's method, more or less, the existing value in the interior vein, in so far as the pressure exceeds that in the interior of the eye, that is to say, in so far as there is no independent "false" pulsation.

I will now pass on to describing arterial pressure. As I have already mentioned in the foregoing, it is necessary to distinguish physiological pulsation depending on arterial pressure movements caused by "pulsation" as a result of pressure. The physiological pulse in the eye is a manifestation well known since long ago, but interpreted quite erroneously, and is, indeed, due to diseased changes in the arterial system, *e.g.*, in aneurysm of the aorta, in insufficiency of the valves of the aorta, and in Graves' disease. But even in these pathological cases there has been nothing further added to the knowledge of this phenomenon. Indeed, this phenomenon has become the order of the day. As stated in the foregoing, it is suggested by the theory on the pulse that the artery must dilate and contract. Should we be unable to perceive this, it is *not* the pulse. The arterial pressure movements, the *true* pulse, are a manifestation unknown as a factor. As a direct consequence of this, there occurs daily a succession of arguments among ophthalmologists hypnotized by the theory on the pulse. As I have indicated before in Part I of my article, we perceive these arterial pressure movements, by selecting a suitable method of observation, in, more or less, 80 per cent. of ocular examinations. By no means, therefore, does the circulatory system in pathological cases serve our purpose in this respect.

As I have already emphasized, we find that also in cases of a rapid pulse in insufficiency of the valves of the aorta, there result these pressure movements in a slightly different way, which is an exact proof that they express the physiological pulse.

Only the physiological pulse, therefore, which is entirely analogous with the pulse of the arterial system, can be an indication of retinal arterial pressure. For the carrying out of measurements, however, it will be necessary, as already stated, to exercise pressure on the eyeball artery in order to observe when the arterial pulse diminishes (diastolic pressure) and when it ceases (systolic pressure). This for easily comprehensible reasons is impracticable, not only because of technical difficulties in accomplishment, but also owing to the difficulty in perceiving this pulse.

I am not aware of the behaviour of the physiological pulse in the animal eye, as I have not carried out any investigations to that effect.

In consideration that pressure exercised on the eyeball artery is impracticable, it would perhaps be apt to question whether there is any pressure on the *eyeball* to replace it. Under such pressure it would be possible to observe the physiological pulse with accuracy, both its weakening and its disappearance. This method would not give the anticipated results. By exercising pressure on the eyeball, we change the physiological conditions of pressure ruling in the system of retinal blood vessels. The *physiological* pulse cannot therefore, so far as it can be judged, in connection with pressure on the eyeball, be an indication of physiological pressure in the retinal artery.

There still only remains the "pulse," due to arterial pressure. Can *this* serve the purpose of a factor for ascertaining arterial pressure, and therefore be the pulse suggested as such by A. v. Graefe nearly a century ago, and even to-day passes as such? In other words, does the result due to pressure on the arterial "pulse" permit us of ascertaining in the retinal artery physiological systolic and diastolic pressure?

*But, above all, it is necessary to ascertain what this pulse is and how it behaves.*

As we have already repeatedly stated, the pressure "pulse" does not in any way remind us of the physiological pulse. It consists of two phases: The first phase, arterial contraction, and the second phase, arterial dilatation. The first phase is rapid, the second slow. A. v. Graefe gives a definition of arterial systole and diastole which coincides with the definition given of cardiac systole and diastole. No doubt, the arterial movements remind us of the functions of the heart. But whence this sudden resemblance of the artery to the heart, and this at one particular spot in the vicinity of the disc? The contraction and dilatation of the blood vessel depend on the sympathetic nerve. Exactly the same phenomenon can be observed in the ears of rabbits. Due to excitation of the nerve, the artery contracts, and when this excitation ceases—it dilates. However, the rhythmic movement of contraction and dilatation due to cardiac systole and diastole, and also in pressure "pulse," we do not observe anywhere under the influence of *nerves*.

Is therefore arterial pulse due to pressure? As in cardiac systole, we see that there appears a gliding movement in the artery, which, subsequently, during the diastole, returns to its original position. We notice the same thing in subcutaneous arteries as we stated in the first place.

It would follow from v. Graefe's interpretation that from the moment when the cardiac systole takes place, the blood stream reaches the retinal vessels by overcoming obstacles in its way. This would mean that the blood stream must induce arterial dilatation, which, later, gives way to contraction during the cardiac diastole.

In the meantime we have proved that the artery gives way to contraction during cardiac *systole*, and *dilates* during the diastole, the former phase, *i.e.*, the arterial contraction being rapid, and the latter phase, *i.e.*, the arterial dilatation, slower. It cannot so far be ascertained whether the wave making its appearance due to cardiac systole is the original cause of the throb of the arterial pulse, because this throb depends on the *contraction* of the artery. If the systolic wave from the heart were to be reproduced, the first condition would be a *dilatation* of the artery.

The arterial "pulsation" evident at pressure cannot be anything else than passive pulsation, and is therefore a "false" pulsation produced in the same way as "false" venous pulsation with rhythmic pressure palpitation in the eyeball.

In evidence of my proof, I quote an apt remark with which I have not hitherto met with references in the literature.

It refers to congestion of the central retinal artery. In a case of this kind where there occurs pressure on the eyeball, we observe, at the same time, arterial "pulsation." This "pulsation" is altogether identical with pressure pulsation in a normal eye. However, it embraces only a small part of the entire arterial region. *In an artery, therefore, not reached by the blood stream, because it is plugged off (to a great extent), there can be produced "pulsation."* This "pulsation" can only be passive "pulsation" as resulting from pressure palpitation in the eyeball.

Such also would be the state of things in connection with the problem of the so-called arterial pulse. We are now faced with the following problem: This manifestation of arterial pulse somehow cannot indicate to us the amount of diastolic and systolic pressure, because—as I have pointed out—this difference is immeasurable, and, in any case, must be an expression of the pressure conditions in the arterial system of the eyeball. The result obtained by Bailliart's apparatus shows us the impetus needed to exert pressure on the central retinal artery. Can this measured force also serve as a measurement of pressure in that artery?

Wishing to give a reply to this question; let us first examine the mechanism of the actual state of the pulsation, not by beginning with the final phase, but from the very commencement of the experiment undertaken. By exerting pressure on the eyeball, we first observe the "venous" pulsation in the vascular funnel, in so

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far as there has not already occurred pulsation previously. When measuring the pressure, we close the vein.\*

At the same time, the disc becomes colourless (this is not quite visible). The artery begins to "pulse," and in a number of instances these "pulsations" have also included the vein, usually in alternation with the artery.

In the first place, therefore, the venous tube is closed. Although this conclusion is unquestionably imperfect, it suffices to check the normal outflow of blood, the vein in question being a terminal vein. In consideration of the fact that the outflow has been checked, it is necessary to discontinue the incoming flow as well. This, however, need not be proceeded with immediately, due to the capacity of the venous and precapillary-capillary system. The latter, however, is also subjected to pressure. A corresponding pressure of very much longer duration is required by the retinal artery to reach the pressure in the ophthalmic artery. However, any blood stream must not make its appearance in the central artery. Between the tightened vein and the central eyeball arterial branch of the ophthalmic artery, the blood stream will either stop completely or move on very slowly, forcing itself through the tightened vein with great difficulty.

By now increasing the pressure force on the eyeball, there begins, at a certain moment, to reveal itself the first throb of pulsation in the artery. The force to be used in order to produce these manifestations, i.e., the pressure measured on the basis of

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\* The closing of the vein by pressure on the vascular funnel is comprehensible, as it is performed on the spot where the vein possesses the lowest pressure. On the other hand, it is more difficult for us to understand why *arterial* pressure becomes evident in the vicinity of the vascular funnel. The pressure must first be exercised where there exists the lowest pressure, namely, in the ramifications of the arterial circulation.

According to the laws of hydrostatics, the pressure exercised in the closed vessel spreads uniformly to all vascular walls. This pressure should therefore reveal itself first in the ramifications of the arterial circulation wherever the resistance happens to be the lowest. Why such is not the case is hard to understand. Why is the region in the vicinity of the disc more yielding to pressure, and why is pressure not exercised uniformly on all arterial ramifications in that region? Here, indeed, we are confronted with questions which only can be answered conjecturally. One might, of course, be able to prove that the minor arteries possess more power of resistance than the major ones. It should further be indicated that we also measure the reaction to blood pressure by the resistance of the vascular walls the value of the resulting measurements of which in regard to blood pressure, notwithstanding the inclusion of factors of resistance as suggested by Fritze, has been very much minimized.

It is difficult to be satisfied with the universally accepted view on pressure by forcing a glassy substance into the vascular funnel in order to produce "pulsation" and to check the veins. By that pressure we measure uniformly the outflow on every square millimetre of the wall of the eyeball. The pressure, therefore, on the vascular funnel exceeds that on any part of the retina. However, the problems which I have just indicated, are not very essential. Yet, after all, it is a correct deduction, and, at any rate, it is shown that pressure is capable of giving rise to "pulsation" and to contraction of the blood vessels.

Bailliant's scale plus the eyeball pulsation, indicates to us the pressure in the ophthalmic artery, but not the pressure exercised in the central retinal artery. The former we measure according to Bailliant's scale, and the latter can be calculated, as I wish to mention here, by the rhythmically moving pointers on Schiötz's tonometer (2—3 Hg).

It would still be necessary to explain the simultaneity and alternation of arterial and venous "pulsation," which sometimes occurs due to contraction of the central vein. I believe the matter is simple enough provided that the arterial pressure and checked vein are in harmony, and if so, the pulse in both vessels is simultaneous, provided, of course, that the pressure differs in both or, in other words, that there is an alternating "pulse," i.e., the same movement in the intra-ocular pulse, first, vascular contraction at a minimum of tension, followed by contraction at increased tension.

Moreover, the "pulse" manifestations and the relation between the arterial and the venous "pulse" may depend on different factors, such as, for instance, the anatomical vascular system, the pressure rate, etc. Should the pressure in a given vein be very high, then any "pulsation" in that vein is entirely out of the question. However, wherever a "pulse" occurs, it is entirely passive, that is to say, produced by an exterior force acting on the vessels. By summing up the above results, I am able to state the following:—

When exercising pressure on the eyeball, there occurs a contraction of the central vein, and due to this circumstance the flow along the whole extent of the central artery as coming from the ophthalmic artery through the medium of capillary vessels, encounters complete restraint or, at least, a substantial check. The blood stream arrives at a standstill. There now results an equilibrium between the pressure in the ophthalmic artery and that in the central retinal artery. In proportion to further pressure, there occurs in the artery a "pulse" consisting of two phases. The first rapid phase is due to arterial contraction, and the second more lasting phase to arterial dilatation. These movements are passive, being produced by the throbbing pressure in the eyeball. This is exactly the same thing as happens in venous "pulsation." The force needed in order to produce the first throbbing "pulse" consists of three factors: (1) eyeball pressure; (2) pressure exercised by Bailliant's apparatus, and (3) pulsation of the eyeball artery. As regards Bailliant's method, we can therefore measure with more or less accuracy the pressure in the ophthalmic artery, but not in the central retinal artery.\* The difference between

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\* Seidel has also written on this point.

the pressure in the ophthalmic artery and that in the central retinal artery—we must confess—is known near enough, seeing that the central artery is considerably narrower than the ophthalmic artery, and, according to the laws of physical pressure applied to the liquid passing from a wider tube to a narrower one, it diminishes considerably. Thus the dynamometer test affords us the possibility of determining the approximate pressure in the ophthalmic artery, but in any gradual pressure it differs from that in the central retinal artery for the determination of which we have no means at our disposal.

Summing up all our results in brief, we are in the position to state as follows: The arterial "pulse" as well as the venous "pulse" is a passive pulse produced by a rhythmic throb due to eyeball pressure. The blood stream in the vein is uniform, circulating without any oscillations due to pressure, so that there is no difference between diastolic and systolic pressure. Due to a fundamental error of Bailliant's method, pressure pulse has been identified with spontaneous pulse. A spontaneous pulse in the retinal artery comes nearer the truth. It can be observed in 80 per cent. of quite healthy individuals who are not suffering from circulatory disturbances. The result turns out to be different in cases of rapid pulse. This depends on the rhythmic onward thrust of a section of the artery, due to cardiac systole, in the same way as the pulse in other arteries. However, only adequate experience in the observation of spontaneous pulse could afford us an answer to the question of pressure in the retinal vascular system. Unfortunately, such experience is humanly impossible.

The methods of investigating pressure in the brachial artery cannot be adopted for the measurement of pressure in the retinal blood vessels. The pressure on the eyeball creates entirely different circulatory conditions, so that there is no analogy between these two methods. Considering that the physiological arterial pulse is hardly perceptible, the difference between systolic and diastolic pressure is practically nil, and is therefore not capable of being measured. If conditions were such as suggested by Bailliant and others, *i.e.*, 0.45:1, the spontaneous pulse in the retinal artery would necessarily be seen in every eye at once, and would necessarily be more distinct than the above mentioned arterial pulse, where this proportion amounts to 0.6:1.

By Bailliant's method we are able to investigate the height of retinal venous pressure, in so far as the vein does not present independent "pulsation," *i.e.*, "pulsation" occurring already without pressure. Bailliant's method does not enable us to estimate pressure in the central retinal artery, but we can thereby

determine the approximate pressure existing in the ophthalmic artery.

In consideration that the central retinal artery is considerably narrower than the ophthalmic artery, the pressure in it must necessarily be considerably lower, which, however, cannot be determined even approximately.

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## PTERYGIUM\*

BY

EMANUEL ROSEN

NEWARK, N.J.

THE great number of operations devised for pterygium, like the many operations proffered for ptosis, bespeaks the frequency of failure in this surgical condition. Recurrence in pterygium operation is the rule in the hands of the experienced, as well as in those of the novice. Having seen a great many pterygia in the past 2½ years, among which were included a rather large number of recurrences, it became increasingly apparent that the usual method of surgical treatment, namely, the McReynolds transplantation, was not functioning too well in the hands of many ophthalmologists. This procedure was the operation of choice of many ophthalmologists with whom I spoke and most men readily agreed that recurrences were all too common. Each seemed to have one modification or another, but all used the McReynolds operation as the basic procedure. It is true that in a good many cases a follow-up was rather difficult, so that the final result was not adequately obtained. McReynolds<sup>1</sup> has stated that his operation was a modification of the Desmarres<sup>2</sup> procedure, the feature which he introduced being the closure of the exposed sclera following the separation of the pterygium. McReynolds believed that if a break in the conjunctiva occurred in the axis of the palpebral fissure, the results would be more or less unsatisfactory, for the insertion of sutures bringing the divided parts into apposition is bound to produce some thickening, and irritation consequent upon these conditions will serve to excite the neighbouring subconjunctival vessels, and thus cause a return in growth of the pterygium. "By concentrating the vascular activity underneath the lower lid where the pterygium is not only removed from view, but protected from irritating influences of dust and exposure, the process of atrophy naturally and

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\* Received for publication, May 5, 1947.



FIG 1.

Shows a typical moderately advanced pterygium of characteristic appearance before operation.



FIG 2.

Shows the same eye approximately two months after operation.

surely follows." It does not seem justifiable to assume that conjunctival approximation cannot be attained adequately in the midline, for in a great many operations the site of union is soon not recognizable. Again "vascular activity need not be concentrated in the lower cul-de-sac"—burial into the squamous-like caruncle would seem to be a much more compatible histological union. McReynolds also emphasized the importance of complete removal of the head of the pterygium with a sharp knife, suggesting that any technique of divulsion should be avoided. The knife should be as sharp as possible and no attempt should be made at tearing the pterygium head from the cornea. This point is worthy of re-emphasis, especially in view of a recently reported operation in the Navy Medical Bulletin<sup>2</sup>.

### Pterygium operation

*Technique.*—The head of the pterygium is grasped with forceps as in any operation for pterygium, and is carefully dissected off the cornea to the limbal area with a sharp knife. The conjunctiva is then separated from the limbus both above and below the pterygium for a distance of three mm. and undermined from the limbus to the region of the newly retracted pterygium head. (It seems that upon undermining the conjunctiva in this area after separation at the limbus, the pterygium also retracts). A double-armed suture is then inserted about 1 mm. from the head of the pterygium going from conjunctival to episcleral surfaces with the thread coming into position vertically. The pterygium is then folded back upon itself so that episcleral tissue is in contact with episcleral tissue and the double-armed suture is brought out through the centre of the caruncle, the needles coming through at 2 mm. vertical separation. The caruncle is punctured with some difficulty, this procedure being slightly painful. The episcleral tissue below the pterygium should be undermined carefully and completely, so that no adhesions hold back the folded pterygium. The suture is then pulled tightly and tied over a small rubber button. This process of folding the pterygium back upon itself produces a tendency toward knuckling of tissues which varies with the broadness of the central portion of the pterygium, and is the one objectionable feature. However, if the pterygium is quite broad, after the head is dissected off the cornea two parallel incisions may be made in the pterygium base separated by a distance equal to the width of the mid-head of the pterygium, and running horizontally for several mms. before folding the pterygium back upon itself. The edges of the conjunctiva are sutured together in a horizontal line starting from the buckled end of the pterygium and going to the limbus. The last conjunctival limbal suture should be placed very carefully and cut quite closely so that no suture ends impinge upon the cornea. 6-0 silk should be used for these sutures. Usually three or four sutures are required to close the conjunctiva completely.

This procedure is adequate and not at all difficult to perform in the mild types of pterygium, but may also be used in the more disturbing recurrent variety. The procedure is much the same although in one instance it was found to be of distinct advantage to use two double-armed sutures, one being brought out at the caruncle and a second coming through the structure of the pterygium itself. The small rubber button prevents the suture from sliding back into the folds of the conjunctiva where difficulty

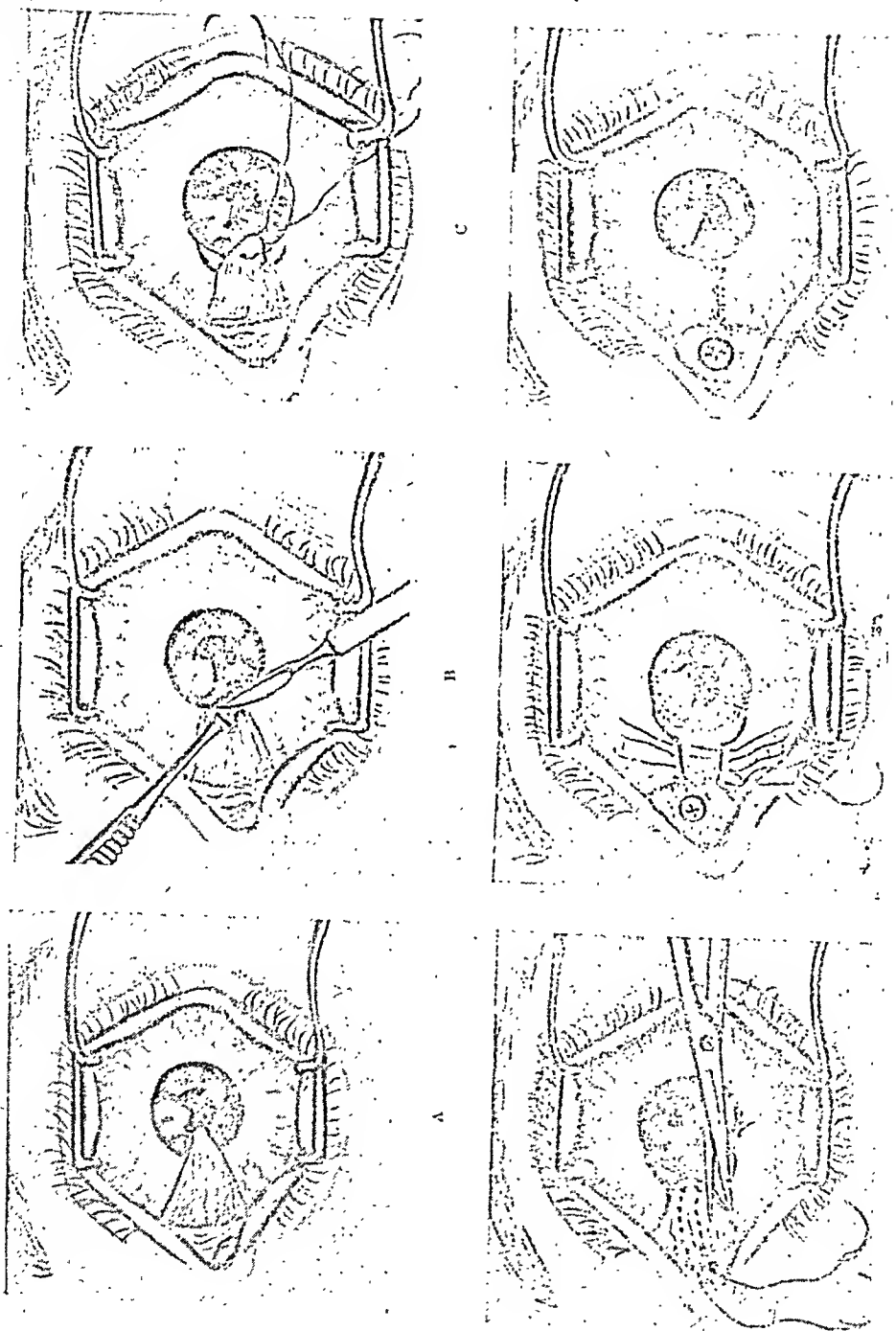


FIG. 3.

This is a diagrammatic representation of the various steps in the operation for pterygium. (a) Characteristic pterygium before operation. (b) Pterygium being severed from the cornea and dissected back to its base. (c) Double armed suture placed through pterygium head and emerging from the episcleral side. A small area of conjunctiva is undermined at each limbal area and appears like a small crescent. (d) Each arm of the suture is passed underneath the pterygium and brought out through the caruncle. The pterygium is separated from the sclera with the scissors at its upper and lower borders. (e) The double armed suture is tied over a small rubber button. The upper and lower free edges of the conjunctiva are sutured with three or four single sutures. (f) The conjunctiva is completely approximated.



is usually encountered in removal, and frequently requires cutting down into the conjunctiva. This suture may be retained for ten days. The other conjunctival sutures usually work out readily. A moderate amount of secretion exists for several days but may be handled adequately through the use of hot compresses. The patient experiences some discomfort for two or three days and the operation should be regarded as a major procedure for that post-operative period.

During the past seven months twenty-five cases have been treated in this manner, in which time there has been only one recurrence. These cases have only been followed from two to six months, but in many instances the appearance at the end of two months seems to indicate that there will be no recurrence for the caruncle flattens out, the conjunctiva unites evenly and the opaque cornea becomes thinned out. In the single instance where the result was not considered very satisfactory, the patient had previously been operated upon twice and the involved tissue was hypertrophied and fleshy. There was overlapping and redundancy of tissue after the pterygium was folded back upon itself. Two weeks after the operation the redundant tissue was cauterized with silver nitrate and several days later the appearance was regarded as most satisfactory.

The advantages offered by this type of operation are as follows :

1. The head of the pterygium is brought in contact with the modified cutaneous structure, the caruncle, a structure with which the stratified pterygium appears to be compatible.
2. Episcleral tissue tends to fuse with episcleral tissue (produced by folding of pterygium).
3. The direction of growth of the pterygium is completely reversed.
4. An interposing bridge of conjunctiva is placed between the folded pterygium and the corneal focus.
5. Undermining the conjunctiva at the limbus tends to relax the pull upon the pterygium and prevents overhanging of the conjunctiva at the limbus.
6. Since temporal pterygia are extremely rare they need not be considered.
7. The pterygium is completely buried and is no longer exposed to direct elemental irritation.

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## ANTERIOR LENTIGLOBUS

### An Atypical Case \*

BY

K. SEN

CALCUTTA

ANTERIOR lenticonus is a very rare condition. It consists of a small conical projection of the lens at its anterior pole.

Anterior lentiglobus is also very rare. It consists of a small globular projection of the lens at its anterior pole. The projection is a part of a sphere and in lenticonus it is part of a cone.

In both cases the projection consists of clear cortex only. The nucleus remains intact and undistorted (Feigenbaum, 1929; Kienecker, 1929). The projection takes place after birth otherwise the nucleus of the lens would have been affected; however, Seefelder and Wolfrum (1907) noted it in a foetus of 4 months. The projection is in the pupillary area. It usually occurs as an anomaly without any other changes in the eye.

The lens itself is transparent. On examination with the ophthalmoscope a dark disc is seen in the centre of the pupillary area

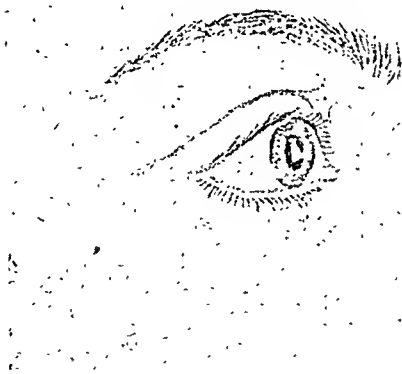


FIG. 1.

Anterior lenticonus (Duke-Elder).

"resembling in appearance the effect produced by an oil globule in water: this is due to the fact that none of the rays from the fundus reaches the observer's eye owing to prismatic reflection in the axial region" (Duke-Elder, 1938), Figs. 1 and 2. As the projection has

\* Received for publication, September 23, 1947.

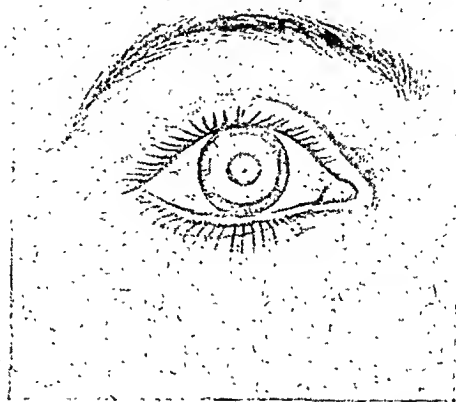


FIG. 2.

Anterior lenticonus as seen by the plane mirror of the ophthalmoscope (Duke-Elder).

an increased curvature the area is highly myopic ( $-20.0$  D., Kienecker, 1929). The projection has always a tendency to increase. Feigenbaum (1932) followed up a case for six years and recorded that the projection increased in curvature making the area more myopic, the increase being from  $-5.50$  D. to  $-10.0$  D. As long as the capsule remains intact the projection of the lens remains transparent. Eventually an anterior polar cataract develops (Jaworski, 1910; Tsukahara, 1930; Feigenbaum, 1932), most probably due to the rupture of the lens' capsule from overstretching.

The cause of this condition is not definitely known. A delayed separation of the lens' vesicle (Krusius, 1910), an inflammatory adhesion to the cornea (Mohr, 1910), have been suggested. Collins (1910) suggested that the normal suspensory ligament in its development exerted chief traction on the anterior capsule and the absence of such traction might account for anterior lenticonus. Mann (1937) noted that in some lower animals the lens appeared to bulge through the pupil as though the iris was pressing it back at the periphery, and suggested that it was possible that some such deforming stress might have occurred in foetal life owing to a too rigid pupil so that the lens had been permanently moulded.

The following case shows some very unusual features.

A. S., a Sikh boy, aged 14 years, was seen on October 1, 1946. He complained that on waking up on the morning of September 28, 1946, he discovered that he did not see well with his right eye. He was a tall, well developed boy. His physical examination revealed no abnormality. His father was seen and he showed no abnormality.

On enquiry from his father it was noted that there was no abnormality in the bodies and eyes of the boy's mother, brother and two sisters. There was no history of trauma to the eye of the boy.

On examination of the right eye the conjunctiva, cornea, and anterior chamber were normal. Pupil was reacting well to light and accommodation. There was a very small opacity on the anterior surface of lens at its upper and inner quadrant and the opacity was mostly covered by the edge of the pupil. The central part of the pupillary area seemed to be quite transparent. The tension was normal. The vision in the right eye was 5/60 and

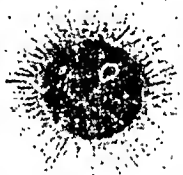


FIG. 3.

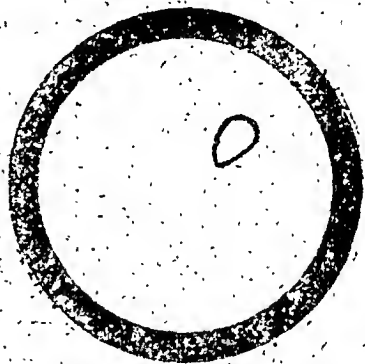


FIG. 4.

there was no improvement with glasses, but on contracting the pupil with eserine the vision improved to 6/24 (+1) with  $-2.0$  D. The vision in the left eye was 6/6 with  $-2.75$  D.

On dilating the pupil the size of the opacity was found to be approximately 3 mm. by 2 mm. (Fig. 3). On examination with lens and loupe the small opacity on the lens was found to be really a tiny little projection of the anterior surface of the lens; the centre seemed to be transparent and the margins were grey. It was egg-like in shape, its longest axis being in the 1 o'clock—7 o'clock meridian, the broad part being towards 1 o'clock and the narrow end towards the centre of the pupil. With transmitted light (Fig. 4) the centre was found to be transparent and the edges were opaque. With slit-lamp (Figs. 5 and 6) it was found that the projecting part consisted of a herniation of the anterior cortex of the lens through an egg-shaped rupture of the capsule the edges of which could be seen surrounding the herniation and were curling forward. The capsule over the projecting part was thought to be deficient. The surface of the projection was irregular and was pitted at the lower and outer part. There were several lines of tension on the capsule of the lens from the narrow end of the ruptured capsule spreading

over the pupillary area. This probably explained why the vision could not be improved beyond 6/24 (+1). The curvature of the projection was spherical and not conical. The other parts of the lens including the nucleus were normal. There were no myopic



FIG. 5.



FIG. 6.

changes in the fundus. There were no other abnormalities in the eye either congenital or acquired, inflammatory or abiotrophic.

A short description of the case and the paintings of the lens condition were sent to Prof. Ida Mann, and she has very kindly sent the following remarks, "Embryologically I cannot explain it at all, though I do feel that one cannot be certain of the complete absence of the capsule over the bulge. If this had been the case I should have expected the lens fibres to have become opaque and partially dissolved. I think therefore that there must be a very thin layer of the deep lamella of the hyaline capsule and it is the zonular

ella which is absent over the bulge and everted around the base. That could have produced this I have no idea, though probably prima at or soon after birth might account for it."

The case was again seen in January, 1947, *i.e.*, three months later. The condition was found to be exactly the same. No opacity of the lens cortex had developed and there was no increase in the size of the projection. The vision was still the same.

### Discussion

Embryologically the lens capsule is composed of two layers. The inner layer is secreted by the cells of the lens vesicle and the superficial or zonular layer is added later on the outside of this in the

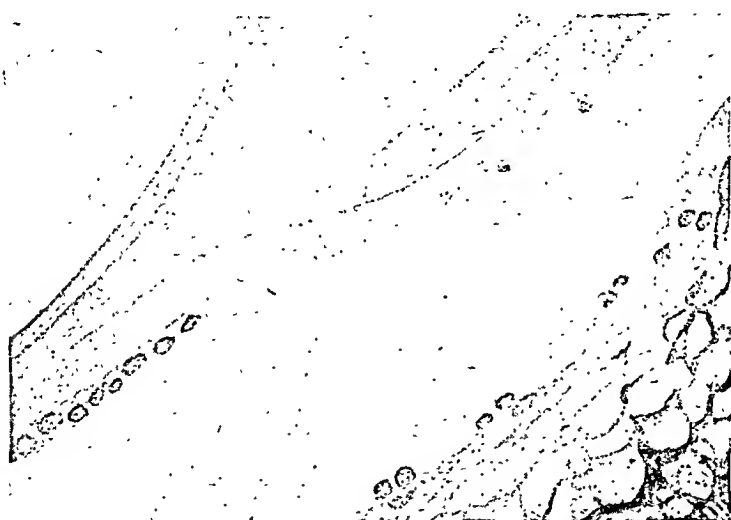


FIG. 7.

The lens capsule (Tooke)

peripheral part and is formed by the coalescence on the lens of the fibres of the suspensory ligament (Mann, 1937). Histologically two layers can be demonstrated either by staining with aniline blue (Cauvieux, 1922) or by use of a silver impregnation method (Busacca, 1929). Tooke (1933) demonstrated that each of the two parts of the capsule was divided into separate layers (Fig. 7). Vogt (1925-32) and Elschnig (1929) believed that the zonular lamella extended completely over the anterior surface, while Busacca (1929) claimed that there were three different structures, a zonular lamella confined to the lateral portions of the lens, a fine pericapsular membrane surrounding the entire lens and a capsule proper composed of several layers.

In this particular case, the lens capsule, except a very thin lamella of the deep layer, was ruptured and the edges were curling forward. Although under the slit-lamp no capsule could be demonstrated over the herniated area (Fig. 6), a thin layer must be present otherwise, as Prof. Mann pointed out, there would have been opacification and partial absorption of the lens fibres.

The curvature of the projection was regular and spherical. The surface of the projection presented a most interesting appearance (Fig. 5). The surface was pitted. This was specially apparent at the lower and outer part of the projection. This appearance has not been seen or described in cases of exfoliation of the zonular layer of the lens capsule. This appearance is very difficult to explain.

Too much reliance cannot be placed on the history of sudden onset of dim vision as many cases even of amblyopia ex anopsia state that the dimness of vision in the particular eye is of a few days' or weeks' duration.

In the absence of any other abnormality either congenital, acquired or abiotrophic, one would like to suggest that the condition was due to a congenital weakness of the lens capsule and most of the layers gave way either spontaneously or during a very trivial trauma allowing a herniation of the anterior cortex. It does not seem possible to postulate when the rupture took place.

### Summary

A case is described in which there was a tiny herniation of the anterior cortex of the lens through an egg shaped rupture of the superficial layers of the anterior lens capsule.

The cases of anterior lenticonus and anterior lentiglobus described in the literature showed the projection of the anterior cortex to be either conical or globular in shape. They were round and situated at the anterior pole of the lens occupying the pupillary area. The capsule over the projection was intact especially at the early stages. In this case, most of the layers of the anterior capsule of the lens were already ruptured and the edges were curled forward. The herniation of the anterior cortex was egg-like in shape, was eccentric in position and the surface was pitted.

It seems that a case like this has not previously been reported. It was intended to report this case after keeping the patient under observation for at least one year. When he was sent for in March, 1947, it was found that he, with his family, had left for his home in the Punjab. In July, 1947, he or his family had not returned and their whereabouts were not known. (Note.—Severe communal riots broke out in the Punjab in March, 1947).

All French and German references have been taken from Duke-Elder's Text-Book of Ophthalmology.

Finally, thanks are due to Major E. J. Somerset, I.M.S., for help in preparing the paper and also for some useful suggestions.

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## ON GENESIS AND OPERATION OF SENILE ENTROPION

BY

-Prof. A. KETTESY

DEBRECEN

CONTRARY to cicatricial entropion with anatomical changes of the intermarginal surface and of the tarsus, senile (or, as it is sometimes called, spastic) entropion is a simple turning in of the unchanged tarsus of the lower lid.

Under normal conditions the lower lid (correctly its skeleton: the tarsus) is kept in right position by two forces: (1) by the elasticity of the tarso-orbital fascia with the embedded inferior tarsal muscle; (2) by the tone of the orbicularis muscle exerting equally distributed pressure upon the lid. The orbicularis muscle plays the more important rôle. Its normal distribution is maintained by connective tissue branching off between the bundles. Other forces such as capillary adhesion and elasticity of the skin are of less importance.

In senility there is sometimes a slackening of the whole palpebral connective tissue, creating a situation ready to result in entropion: drawing up and accumulation of the bundles of the orbicularis in the lid-margin. The lid is in this phase still in its normal position but unbalanced. Every small pressure at the lid-margin in simple



blinking, is apt to upset the equilibrium, when the tarsus is on a sudden turned in, taking with it skin, muscle, and eye-lashes.

We are able to reset the lid into its original position by simply pulling the skin downwards, thus bringing about normal distribution of the orbicularis muscle.

The inhibiting rôle of the tone of the inferior tarsal muscle was shown by Blaskovics. Instilling cocaine and adrenalin, we increase the power of the tarso-orbital fascia, consequently entropion cannot ensue. The result, of course, lasts only as long as the drug is working.

The majority of the operations for senile entropion act on a similar principle: they increase one or several of the various forces, that are keeping the lid in right position.

Surgical operations have been directed towards (1) shortening of the skin (Celsus, Terrien, Snellen, Hotz, Imre); (2) re-establishing the absent pressure on the convex tarsal margin (Graefe, Koster, Birch-Hirschfeld, Montgomery, Goldzieher, Blaskovics and others); (3) The same pressure is obtained by a triangular excision of the tarsus (Muller); (4) Increasing the tone of the tarso-orbital fascia by operative procedure (Tóth, Trantas); and (5) we might add the proceedings, that are combining several of the above mentioned (Blaskovics).

It is a common feature of all groups that they leave unattacked the decisive factor of the turning in: the accumulation of the orbicularis in the margin, or they touch it only secondarily and insufficiently, hence the relapse occurs mostly very soon, or, trying to get a lasting and satisfactory result by increasing the effect, the entropion turns into ectropion.

Out of the described mechanism ensues the fact that the accumulation of the orbicular muscle is terminal. Therefore, from the practical point of view this is the only cause. All the other conditions are only preliminary.

The solution of the problem is excision of the orbicularis muscle of the lower lid without anything further.

It was Hotz who proposed the removal of the palpebral part of the muscle first, as a detail of his well-known operation originally devised for cicatricial entropion. He excised only some bundles in order to make the tarsal surface bare for putting in his everting sutures.

Our procedure consists of a thorough excision of the muscle, the whole palpebral portion as well as the greater part of the orbital section.

**Local anaesthesia.** We put a lid-plate into the lower fornix. Pressing it against the lid, we are able to perform the operation in total bloodlessness.

The skin incision is close below the line of the eyelashes. We

undermine the skin downwards as far as the orbital margin, advancing between skin and muscle. The palpebral part of the orbicularis as well as the lower portion of the muscle is thoroughly extirpated with fine forceps and scissors until tarsus and orbital fascia are clearly exposed.

Sutures are superfluous, for coaptation of the wound is faultless. This little operation gives immediate and lasting result. The muscle being absent, no relapse is possible. There are two parts of the muscle that remain intact: the limbalis and the Riolani, sufficient to maintain normal position and function of the lid.

Over-correction, a delicate point of lid-operations, is not possible. It is well-known that operations for entropion if at all efficacious, easily produce an ectropion, chiefly if there was excision of skin. Removal of skin is in our operation never necessary and therefore absolutely forbidden. Sometimes at the end of the operation the skin appears to be redundant, as it applies itself to the line of the eyelashes in folds. We are not persuaded by this sign to excise the skin, as the consecutive fine cicatrisation smoothes out the skin in a few days.

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## A NOTE ON THE PHYSIOLOGY OF THE AQUEOUS HUMOUR\*

BY

E. BÁRÁNY and H. DAVSON

IN recent papers it has been shown (Bárány, 1947, *a*, *b*, *c*), that the rate of penetration of sodium into the aqueous humour is dependent to only a small extent on the blood pressure. The equilibrium concentration of sodium in the aqueous humour and the osmotic pressure of the aqueous are even less affected by a blood pressure reduction. These results have been discussed in relation to certain possibilities of the mode of entrance of sodium, namely:—

(*a*) Secretion in accordance with an equation based on certain assumptions (Kinsey and Grant, 1942).

(*b*) An ultra-filtration process involving an actual bulk movement of fluid.

The possibility of a simple diffusion mechanism as envisaged by Davson and Quilliam (1940), appeared to Bárány to be excluded by Kinsey and Grant's work. The conclusion was reached that bulk movement of fluid was a negligible factor in the penetration of sodium and in the formation of the aqueous humour generally and that the rate of flow of aqueous was only little affected by the intra-ocular pressure.

We should like to emphasize the dependence of these conclusions upon the validity of the interpretation by Kinsey and Grant of their own results, an interpretation not accepted by Duke-Elder and Davson. The papers by Bárány have been criticised recently by Davson (1947) in this light but there are a few corrections that must in fairness be made. The statement by Davson "The notion that a molecule or ion may not enter by simple diffusion but may enter by ultra-filtration has no physical meaning" is indeed ultimately true of any membrane system; nevertheless the conditions may be such that quantitatively the penetration of a substance by simple diffusion may be small in comparison with that entering by ultra-filtration. Thus, if salts could only penetrate the eye membranes in a strictly limited region and if, moreover, filtration from the blood took place only in this region, and consisted in a continuous flow into the eye, it could be stated that sodium entered predominantly or perhaps exclusively by a filtration process, simple diffusion being excluded by the impermeability of the major part of the membrane to this substance. Such a system was, in fact, envisaged by Bárány, although this was not explicitly stated. Bárány's experiments actually exclude this mechanism since the rate of penetration of sodium was almost independent of pressure.

One other point should be mentioned. Davson objected to the use of a mean value not significantly different from unity. It is agreed that this value was not statistically different from unity but it should have been pointed out that exactly the smallness of this difference was in favour of the general argument.

In conclusion, perhaps it is worth devoting a few words to the general problem of whether salts are actually secreted into the eye or whether they may enter by simple diffusion. Kinsey and Grant's "secretion equation" is very similar in form to the simple diffusion equation of Davson and Quilliam; it is not impossible that their data would fit a correct dialysis equation equally well as they actually fit their "secretion equation." The "dialysis equation" of Kinsey and Grant must be unrealistic, as pointed out by Duke-Elder and Davson (1943)<sup>†</sup> and therefore it is not surprising that it does not fit their data.

The problem of the secretion of salts into the eye is thus still in a state of flux; it would appear that a mere mathematical analysis of the data already to hand is not sufficient for a decision.

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<sup>†</sup> According to a personal communication to Davson, Friedenwald is of the same opinion.

## ANNOTATIONS

## Bad Debts

No one can go through his professional life without accumulating a certain proportion of bad debts. Our personal feeling was one of surprise that these were not greater than they were, and it speaks well for the honesty of patients in general that with most of us bad debts are few. Patients of the type of Rawdon Crawley, the arch-exponent of how to live on nothing a year, are always bad debts. Some cases, however, are perfectly genuine instances of the defaulter not having the means to settle his account, owing to financial depression, some sudden calamity or other cause. It might be argued, and with justice, that he should not have chosen that particular moment to consult his oculist. Occasionally the unpaid account is due to sheer laziness and unbusinesslike habits on the part of the recipient. Such people can be brought to book by employing a debt collecting agency or sending a solicitor's letter. But the hard baked non-payer is usually proof against even these. He does not mean to pay and the only way to make him is to institute legal proceedings. For small sums, such as a single consultation, it is obviously not worth while to go to law. Even if the amount is larger, it is doubtful whether the publicity may not do more harm than good in the long run. Our own view was that these people were not worth powder and shot. In one instance we obtained payment of a long standing account by refusing to see any other member of that family till it was settled. The loss of this type of patient does not hurt one's practice.

The patient who pleads poverty and manages to get his surgeon to accept less than the usual fee for an operation is not quite in the same class as a bad debt. We recall an amusing example of such a case in our early days when we were asked to assist at an operation for cataract. On us devolved the duty of instilling cocaine into the eye of a little rat-like personage, who sat on a chair in the corner, in a state of profound melancholic abstraction. Once or twice he looked up at us with his other eye in which we observed a peculiar twinkle of satisfaction. He was a cheap case and his surgeon had learnt, after the question of fees had been settled, that he was really quite well off. This must have been the cause of his twinkle of satisfaction. "I've done you fellows in the eye and am going through with it" was what we imagined it conveyed.

Of other bad debts we remember a young man who had a small corneal abrasion following injury from a tennis ball. He was shocked out of all proportion to the extent of his injury, and we had to provide him with a whisky and soda as well as the appropriate local

treatment. We never saw him again and he never paid his fee and got away with more than one expects to do when visiting a professional man.

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### Amicum pèrdere est damnòrum maximum

The Latin tag which forms our heading says that to lose a friend is the greatest of losses. Among a professional man's oldest friends are the tools of his daily work. The ophthalmoscope one has used for many years is a very old friend indeed and it behoves us to take care of it. We well remember the annoyance of a friend of ours at the loss of the ophthalmoscope he always used. It was a Frost's model and had seen much service. He was going home one afternoon after the out-patient work at hospital was over, and he travelled on the top of a bus. The ophthalmoscope was carried in the tail pocket of his morning coat. Some miscreant picked his pocket and he arrived home without his ophthalmoscope. It was a grievous blow, and it took him some time to get used to a substitute. The moral of this story is that you should carry your tools either in an attaché case or in some pocket not so easily picked as one in your coat tails, if anyone ever wears a morning coat nowadays. Mr. William Lang always carried his ophthalmoscope loose, in sections, in his waistcoat pocket and we never heard of his losing it. The other alternative is to eschew travelling on bus tops.

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## BOOK NOTICES

**The British Orthoptic Journal.** Published annually by Wilding and Son, Ltd., Shrewsbury. Price, 7/6.

The fourth volume of the *British Orthoptic Journal* maintains the high standard set by its predecessors.

It opens with an editorial note describing certain innovations in the *Journal*, such as the invitation to ophthalmic surgeons and to orthoptists overseas to contribute articles and it closes with lists of successful candidates in the 1947 examinations and of the various orthoptic training schools. The body of the *Journal* is made up of some twenty-eight separate papers written by ophthalmic surgeons and orthoptists, a copy of the general and of the detailed syllabus for orthoptic students and an account of the activities of the British Orthoptic Society and of its branches.

The papers are remarkable for their general excellence and for the variety of subjects with which they deal, e.g., "are orthoptics really

necessary"; "accommodative squint associated with emmetropia"; "the adoption of rhythmic illumination for orthoptic treatment"; "a new method of developing normal retinal correspondence"; and "some observations on operation results." There seems to be general agreement among orthoptists that the period of treatment should not be unduly prolonged before the aid of surgery is invoked and in one paper, by an ophthalmic surgeon, it is written that the orthoptist might suggest to the surgeon which muscle or muscles it would be advisable to operate upon. The author says that many surgeons would disagree with the idea but he justifies it on the grounds that the orthoptist has a more detailed knowledge of the case than has the surgeon.

Another point of general agreement seems to be that the period of clinic treatment should be shortened as far as possible. In some papers we are told how to separate the cases which are likely to benefit from orthoptic treatment from those which are not, others deal with the value of homework as supplemental to training received in the clinic and others with procedures for overcoming suppression and abnormal correspondence more quickly than is usual when employing standard methods.

In general, this volume provides evidence of the progressive nature of orthoptics and of the keenness and enthusiasm of its practitioners and we hope it will enjoy the large circulation it deserves among ophthalmic surgeons.

#### **Chronic Ill-health relieved by drainage of the para-nasal sinuses.**

Rosa Ford. Pp. xii and 104. Henry Kimpton, London, 1948.  
Price 6/-. s.

A list of the diseases which the authoress states have been cured or relieved by suitable drainage of the nasal sinuses is, to say the least, formidable. In some ways it is reminiscent of the more adventurous and enthusiastic lucubrations of the advertisers of patent medicines, ranging as it does, from amenorrhoea to strabismus, and from obesity to disseminated sclerosis. Indeed the very universality of her claims does her some disservice, since the chapters on diagnosis, pathology and treatment are reached only after wading through a series of case reports, in which sinus infection, not diagnosed by orthodox clinical methods, is presented as the ultimate cause of diseases for which no other origin can be found, and its treatment as the ultimate panacea.

Reports of forty-seven cases are given in brief; the story is similar in all; ill-health of various kinds, fully investigated with no cause being found; sinusitis diagnosed on the strength, in most cases, of contraction of the visual fields; treatment by inhalations, 50 per cent. glycerine drops, and hydrogen peroxide nasal swabs; discharge from the nose; amelioration or cure. The book may

perhaps do some little service in drawing attention to the possibility of hidden sinus infection as a possible aetiological factor, but the authoress's criteria of its presence, and indications for treatment will hardly command universal approbation.

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## OBITUARY

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### R. D. BEATSON HIRD, M.D., F.R.C.S. (Ed.)

OPHTHALMOLOGY in the Midlands suffered a great loss by the sudden death on March 2, of Robert Dennis Beatson Hird, at the age of 67.

He received his medical education at Birmingham University, graduating M.B., Ch.B., in 1905 and proceeding to M.D., a year later. He obtained the F.R.C.S. (Ed.) in 1909.

Practically the whole of his professional life was spent in his native city of Birmingham, where much of his time was devoted to public work. Among the appointments which he held at various times were: Honorary Surgeon to the Birmingham and Midland Eye Hospital, Honorary Ophthalmic Surgeon to the General Hospital—later amalgamated with the Queen Elizabeth Hospital to form the Birmingham United Hospital, and Ophthalmic Specialist to the Birmingham Education Authority. During the war he served as Midland Regional Adviser in Ophthalmology to the Ministry of Health. He was Lecturer in Ophthalmology to the University of Birmingham until 1945.

Forty years ago he was one of the band of younger men who wrote abstracts for the Ophthalmic Review under the Editorship of E. E. Henderson, and he contributed original articles occasionally to its pages. He also wrote papers in the medical journals and entered into discussions at the Annual Congresses of the Ophthalmological Society; but his literary output was not prolific and it was as a clinician that he was best known.

To all his work Beatson Hird brought those qualities which make for success. To abounding energy were added a deep knowledge and love of his speciality. He had an infinite capacity for taking pains and combined keen observation with attention to every detail. Nothing was too trivial to be noted and no effort too great which would enable an accurate diagnosis to be reached. These methods served as an example to many men now successfully practising ophthalmology in all parts of the Empire. To him ophthalmology was not confined to narrow limits, but was only part of medicine as a whole. The posts he filled on the Staffs of large General Hospitals



R. D. BEATSON HIRD

*La Fayette*





enabled him to exercise to the full his skill in Medical Ophthalmology and his opinion, frequently sought by his colleagues engaged in the wider fields of General Medicine and Surgery, was often of the utmost assistance in difficult cases.

He was a successful teacher. Having an easy and lucid style he was able to leave a clear impression of his subject in the mind of the student.

Throughout the years his enthusiasm remained undiminished. He was ever ready to try new methods and to adopt those which he deemed in any way an improvement on the old.

His services as Midland Regional Adviser in Ophthalmology cannot be over-estimated and it was only his strong sense of duty in those difficult days which compelled him to continue such arduous work following a severe heart attack in the early days of the war.

Outside his profession he was a keen golfer until illness prevented strenuous exercise. He was also interested in astronomy, fond of literature and a discerning philatelist. His collection of rare stamps was amongst the finest and most valuable in the Midlands.

An outstanding personality, Beatson Hird was outspoken and direct, but these qualities were always combined with courtesy and an obvious sincerity. He will long be remembered with respect by friends and colleagues alike and their sympathy is extended to his widow and family.

## NOTES

### Deaths

THE deaths are announced of Mr. Secker Walker, for many years of Leeds, and also of Lieut.-Col. Henry Smith, C.I.E., I.M.S., of Jullundur and Amritsar fame. Mr. Secker Walker was 82 and Lieut.-Col. Smith 91. We hope to publish notices of each in a later number.

\* \* \* \*

### Award

THE Treacher Collins prize has been awarded by the Council of the Ophthalmological Society of the United Kingdom to Dr. H. S. Stannus, for his essay on nutritional eye disease.

\* \* \* \*

University of Glasgow  
Department of  
Ophthalmology  
Spring, 1948

DURING the month of May a series of meetings will be held in the Department on Wednesdays at 8 p.m. The General Arrangements will be similar to the series held last year. Tea will be served after the paper and a discussion will follow. The meetings

will be open to all medical practitioners and senior students interested in Ophthalmology.

May 5—Dr. I. C. Michaelson, "The Growth of Ocular Vessels";  
May 12—Dr. Jas. Hill, "The Disturbances of Lacrimal Apparatus";  
May 17—Dr. W. O. G. Taylor, "Wounds of the Cornea"; May 26  
—Mr. O. M. Duthie, "Cataract Extraction."

\* \* \* \*

**Ophthalmological  
Society of  
Australia**

THIS Society proposes to hold its Eighth Annual General and Scientific Meeting at Perth, Western Australia, on August 15-21, 1948, in conjunction with the Australasian Medical Congress (British Medical Association) Sixth Session.

The organisers of the Meeting are :—Dr. Claude Morlet (President of the above Society), St. George's Terrace, Perth, W.A.; Dr. Bruce Hamilton (President of the Section of Ophthalmology), 174, Macquarie Street, Hobart, Tasmania; Dr. John L. Day (Honorary Secretary of the Section of Ophthalmology), 179, St. George's Terrace, Perth, W.A.

The Society would be honoured to receive representatives of the Section of Ophthalmology, British Medical Association, and would extend to them a most cordial welcome. Intending visitors, however, should contact the Congress Office, 230, St. George's Terrace, Perth, W.A.

\* \* \* \*

**Transactions of the  
Ophthalmological  
Society**

THE Society holds no volumes, or only a limited number, for the following years :—

1898; 1899; 1900; 1901; 1902; 1905;  
1906; 1907; 1909; 1911; 1917; 1918; 1919; 1920; 1921; 1922;  
1923; 1924; 1926; 1927; 1928; 1929; 1930; 1931; 1932; 1933;  
1934; 1935; 1937 (Part I).

It is felt that there may be Members willing to dispose of volumes for these years, which the Society would be grateful to buy at the rate of £1 per volume.

Communications should be made to the Honorary Secretary, 45, Lincoln's Inn Fields, London, W.C.2.

\* \* \* \*

**Medical Celebrating  
Week of the  
Hungarian Medical  
Trade Union**

AN invitation has been received from the President and Secretary General of the Hungarian Medical Trade Union to foreign Ophthalmologists to attend their "Medical Celebrations Week" in Budapest from September 4 to 12, 1948. A preliminary and detailed programme will be published within one or two months.

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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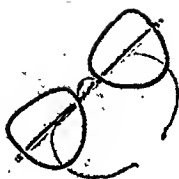
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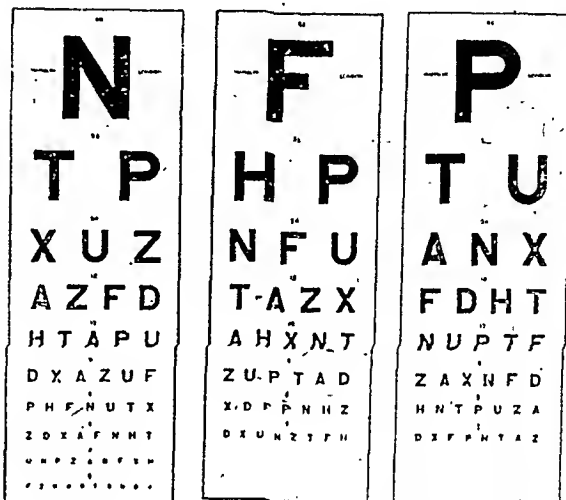


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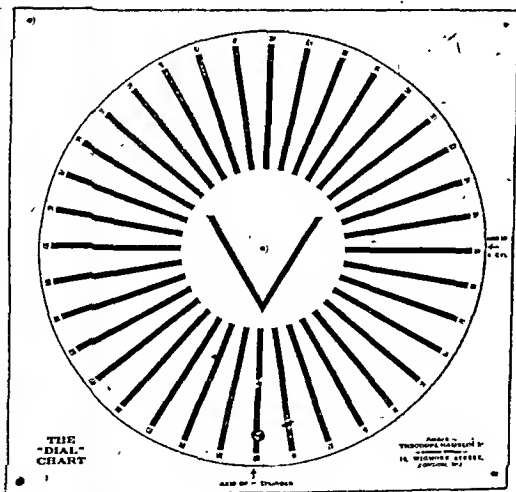
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## COMMUNICATIONS

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### OX VITREOUS HUMOUR. 1.—THE RESIDUAL PROTEIN\*

BY

A. PIRIE, G. SCHMIDT *and* J. W. WATERS

NUFFIELD LABORATORY OF OPHTHALMOLOGY AND DEPARTMENT OF  
CRYSTALLOGRAPHY, OXFORD

WHEN a vitreous humour is removed intact from an eye and put on a filter or hung from a clamp, a viscous fluid drips out of it until finally all that remains is a thin membranous wisp of material. Robertson and Duke-Elder (1933) describe the vitreous humour as "a gel composed of a meshwork of elastic fibrillae suspended in a viscous fluid," and we may suppose that the membranous stuff left after filtration forms the elastic fibrils of the intact vitreous body. This insoluble residue was first studied by Young (1894) and Mörner (1894), who considered that it was collagen because it dissolved in boiling water and the solution set to a gel on cooling. Mörner (l.c.) termed it the residual protein, and it has since been

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\* Received for publication, March 24, 1948.

known by this name. Duke-Elder (1930) described it as like gelatin, but Meyer (1945) classified it as an insoluble mucoid of unknown composition. The analyses of the insoluble residue show that it is a protein. Krause (1934) found 14.16 per cent. N and gave analytical figures for arginine, histidine, lysine, cystine, tryptophane and tryptophane, all of which were present in the material analysed.

The experiments described in this paper bring forward further evidence in support of the view that the residual protein of vitreous humour contains a protein like collagen and describe the liquefying effect of preparations containing the enzyme collagenase on the vitreous body. These results are considered in relation to the well known acid and alkaline shrinkage of the vitreous humour, and are used to formulate a theory of the way in which the residual protein is laid down.

It is difficult to collect sufficient of the insoluble residue from the vitreous humour to identify it by analysis of the constituent amino-acids. One ox vitreous humour with a volume between 12-15 ml. yields only 2-3 mg. of insoluble residue. We have, therefore, attempted to identify this residue through its general properties, by amino-acid chromatography of hydrolysed material, by X-ray analysis and by enzyme analysis. The material appears to be fairly uniform, judged by solubility tests and enzyme digestibility, but we realise that the results we have obtained do not in any way prove that the insoluble residue of the vitreous humour consists of a single substance.

## METHODS

**Material.** The experiments have been done using ox vitreous humours obtained within 1-2 hours after death of the animal. The humours were removed from the eye by making a complete equatorial cut through sclera, choroid and retina and allowing the vitreous humour to fall away from the retina, while still attached to the anterior half of the eye. It was then gently cut and pressed apart from the ciliary body and lens. The posterior lens capsule sometimes adheres to the vitreous humour, but can be removed with forceps.

**Preparation of residual protein from vitreous humour.** The insoluble residue may be separated from the soluble constituents by suspending the humour in saline and allowing the soluble substances to diffuse out into the surrounding fluid. Friedenwald and Stiehler (1935) found that the vitreous humour retained its form during prolonged washing in saline and that when it was finally filtered, the filtrate contained no organic material. We found that if an ox vitreous humour were left in the ice chest in saline

which was changed every few days, all detectable protein and hyaluronic acid had diffused out of the humour within 8-12 weeks. Such washed humours are more flaccid than when fresh and we have taken the insoluble residue remaining after their filtration as the residual protein. Salt may be removed from this by a few days' wash in distilled water.

The insoluble residue may also be prepared by filtration of the fresh vitreous humour followed by washing. This might seem the quicker method, but we found that very prolonged washing, by suspension in saline or water, was necessary to remove the small amount of soluble material remaining after the first filtration of the fresh humour.

*Total nitrogen.* Total nitrogen was estimated in 5-10 mg. samples frozen dried over  $P_2O_5$ . The samples were incinerated with 2 ml.  $H_2SO_4$  + 0.5 g. catalyst (40 g.  $K_2SO_4$ , 10 g.  $CuSO_4$ , 0.17 g.  $SeO_2$ ) incineration being continued for 5-8 hours after clearing. The ammonia was estimated by Markham's (1942) method.

*Total carbohydrate.* This was estimated by the orcin colorimetric method described by N. W. Pirie (1936).

*Hexosamine.* This was estimated by the method described by Elson and Morgan (1933).

*Amino-acid chromatography.* The method of Consden, Gordon and Martin (1944) was used.

### GENERAL PROPERTIES OF INSOLUBLE RESIDUE

The residues from vitreous humour are grey and fibrous, showing considerable tensile strength and some anisotropy, particularly when stretched. When dried, each residue is a dark grey horny string. The colour seems to be due to adsorbed uveal pigment, cotton fibres and dust from the air and from the washing solutions. We found that the total nitrogen of such residues was near 12 per cent. and that they contained no hexosamine and from 3-7 per cent. total carbohydrate. Further purification of the residual protein while it was in this insoluble state was difficult owing to its capacity to adsorb other insoluble materials, such as cotton fibres, etc. From the general properties one may say that the vitreous residue appears to be made up largely of fibrous protein, but we felt that for further purification it was essential to get the protein, or proteins, into solution, even if this involved some degree of hydrolysis. We have, therefore, made a soluble preparation from the vitreous humour residues.

*Preparation and properties of soluble protein from vitreous humour residues.* Ox vitreous humours were washed as free as possible of soluble material by suspension in saline for long periods followed by filtration. The residues from about 50 humours were dissolved in 60 ml. HCl pH 1.8 on a boiling water bath. The cloudy solution was centrifuged and the small black sediment discarded. The supernatant was brought to pH 4 and the small flocculent precipitate that



came out was centrifuged off and has not been further investigated. It seems probable that this is an "artificial mucin," similar to those prepared by Meyer and Smyth (1937) and formed in this case from hyaluronic acid and any of the proteins present. The supernatant fluid from this precipitate was half saturated with ammonium sulphate by addition of an equal volume of saturated solution. An immediate copious precipitate came down. This was centrifuged out, re-dissolved in water and dialysed against distilled water in the ice chest. No further precipitate came out when the supernatant fluid from half saturation was wholly saturated with ammonium sulphate.

After several days' dialysis in the ice chest the solution of the precipitate got by 50 per cent. saturation with ammonium sulphate was frozen and dried. The preparation was a white fibrous material and had a total N. 13.0-13.5 per cent. Further purification by dissolving in warm water, bringing the solution to pH 4, centrifuging and precipitation from the supernatant fluid by half saturation with ammonium sulphate gave a product that formed a firm jelly in the dialysis sac and had no ash, 14.8 per cent. N., no hexosamine and 6 per cent. total carbohydrate. We found that the vitreous humour residual protein lost 3.3 per cent. of its total nitrogen when taken into solution in dilute HCl. This loss probably represents loss of the amide group of glutamine, as Thierfelder and v. Cramm (1919) have shown that glutamine peptides are unstable under such conditions. If we correct for the loss of N on solution in acid the total nitrogen of the soluble product from ox vitreous humour residual protein is then 15.3 per cent.

The characteristic insoluble proteins of the animal body are collagen, elastin and keratin, with reticulin as a rather nebulous substance of unknown composition. The method of preparation and the general properties of the soluble stuff from ox vitreous humour residue suggests that the original material is like collagen and that it dissolves to form gelatin. Solubility in dilute acid is a property of collagen and precipitability by half saturation with ammonium sulphate and ability to form a gel are properties of gelatin. Yet the final value of 15.3 per cent. N. is low for typical collagen or for gelatin. Bergmann and Stein (1939) found that collagen from ox Achilles tendon had 18.6 per cent. N. Few collagens have been analysed, other than those from skin and tendon; Mörner (1894) gave N 17.03 per cent. for ox cornea collagen and we have found that collagen prepared from ox cornea by the method of Bergmann and Stein (l.c.) had N 16.1 per cent. uncorrected for ash.

Both histologists and chemists accept cornea collagen as a typical collagen, so we felt that it would be valuable to compare it in some detail with the vitreous humour material. We have, therefore, prepared a soluble gelatin from ox cornea collagen and have compared its general properties with those of the soluble material from vitreous humour. We have also compared the amino-acid chromatograms of ox cornea gelatin and vitreous humour residues with that of commercial gelatin.

We found that we could prepare a soluble protein from ox cornea collagen by the same method as we had used with vitreous humour residue. This had no ash or hexosamine, total N 15.5 per cent. and 6 per cent. total carbohydrate, and in appearance and

properties was similar to the preparation from vitreous humour. If we correct the total N. for the nitrogen lost on solution in dilute acid, the final figure is 16.0 per cent. total N.

AMINO-ACID CHROMATOGRAM OF OX VITREOUS HUMOUR RESIDUE AND OF CORNEA GELATIN COMPARED WITH COMMERCIAL GELATIN

Collagen and gelatin have a characteristic amino-acid composition. Bergmann and Stein (l.c.) found that ox Achilles tendon collagen contains 26.2 per cent. glycine and 17.1 per cent. proline and Schneider (1940) found 10.8 per cent. hydroxyproline in cow-hide collagen. No other protein so far analysed has such a high simultaneous concentration of these three amino-acids, so that a qualitative analysis, such as is given by an amino-acid chromatogram, may be used to help identify a protein suspected of being related to collagen or gelatin.

The method of partition chromatography on filter paper as a qualitative method of protein analysis was introduced by Consden, Gordon and Martin (1944). The principle is that if a drop of a solution of mixed amino-acids is put on a strip of filter paper and a water saturated solvent is then allowed to flow through the paper by capillary action, the amino-acids will be carried down the paper at different rates, depending on their solubilities in the two phases; water saturated with solvent and solvent saturated with water. They will thus be separated one from another. The presence of the separated amino-acids on the paper can be detected by the usual colour reaction with ninhydrin. A mixture of known amino-acids may be used as a marker solution. Each mixture will give a characteristic pattern of spots which ideally will be separated from one another on the filter paper and one can, therefore, compare one protein hydrolysate qualitatively with another by this technique.

The soluble preparations from ox vitreous humour and cornea were compared with a commercial gelatin (total N. 17.0 per cent.) and with a mixture of glycine, proline and hydroxyproline made up in the proportions in which they occur in collagen. Three to five mg. of each preparation was dissolved in 1.0 ml. 6 N HCl and hydrolysed in sealed tubes at 110° overnight. The solutions were then dried *in vacuo* over H<sub>2</sub>SO<sub>4</sub> and NaOH and all remaining HCl was removed by dissolving the residues again in 1 ml. H<sub>2</sub>O and re-drying *in vacuo*, as before. This was repeated 5-6 times, to be certain of removing all acid.

When partition chromatograms are run on mixtures of amino-acids, the pattern which results when the paper is sprayed with ninhydrin and then heated is characterised by the following features:—

1. The presence of spots at different positions along the length of the run. The exact position of each spot depends upon the nature of the amino-acid component (Consden, Gordon and Martin (l.c.)), and to a certain extent also upon the amount of amino-acid contained in it (Fisher, Parsons and Morrison, 1948).

2. Each spot is coloured. Most amino-acids give spots with ninhydrin which are coloured rose or pink; some, *e.g.*, alanine, are rather more blue, while proline and hydroxyproline are instantly recognised by a characteristic yellow colour.

3. The size of each coloured spot varies. It has been shown that there exists a relatively simple relationship between the area of a spot and the amount of amino-acid in it (Fisher, Parsons and Morrison (l.c.)).

One dimensional partition chromatograms were run on solutions of the hydrolysates prepared as described above from ox vitreous humour and cornea, from commercial gelatin and on a marker solution of a mixture of glycine, proline and hydroxyproline made up in the proportions in which these amino-acids occur in collagen. The dilutions were so made that the volume of each hydrolysate put on the paper was  $3\ \mu\text{l}$  and contained  $30\ \mu\text{g}$  total N. Chromatograms of the three hydrolysates and of the mixture of amino-acids were run on the same sheet so that the pattern would not be affected by such adventitious sources of variation as those due to temperature changes and length of run. The chromatograms were run in two different types of solvent, so that two different types of pattern could be obtained, since the positions of the amino-acids in a developed chromatogram relative to each other and to the solvent front depend upon the solvent used. We used either phenol with 0.7 per cent.  $\text{NH}_3$  or a pyridine-*amyl* alcohol mixture (Edman, 1945).

When the chromatograms were developed very striking similarities in the pattern exhibited by the three hydrolysates were at once evident (Fig. 1). The components in all three mixtures were comparable not only in position but in shades of colour and in spot area. This was true for chromatograms developed in both types of solvent. No attempt was made to identify all the amino-acid components of the hydrolysates, *e.g.*, by running two dimensional runs or by running hydrolysates in parallel with various synthetic mixtures; it was, however, evident that all three hydrolysates contained roughly comparable amounts of proline, hydroxyproline, glycine, glutamic and aspartic acids, and alanine.

Using the one dimensional technique and dealing with complex mixtures of components it is not possible to say whether or not small amounts of other amino-acid residues are present in one of

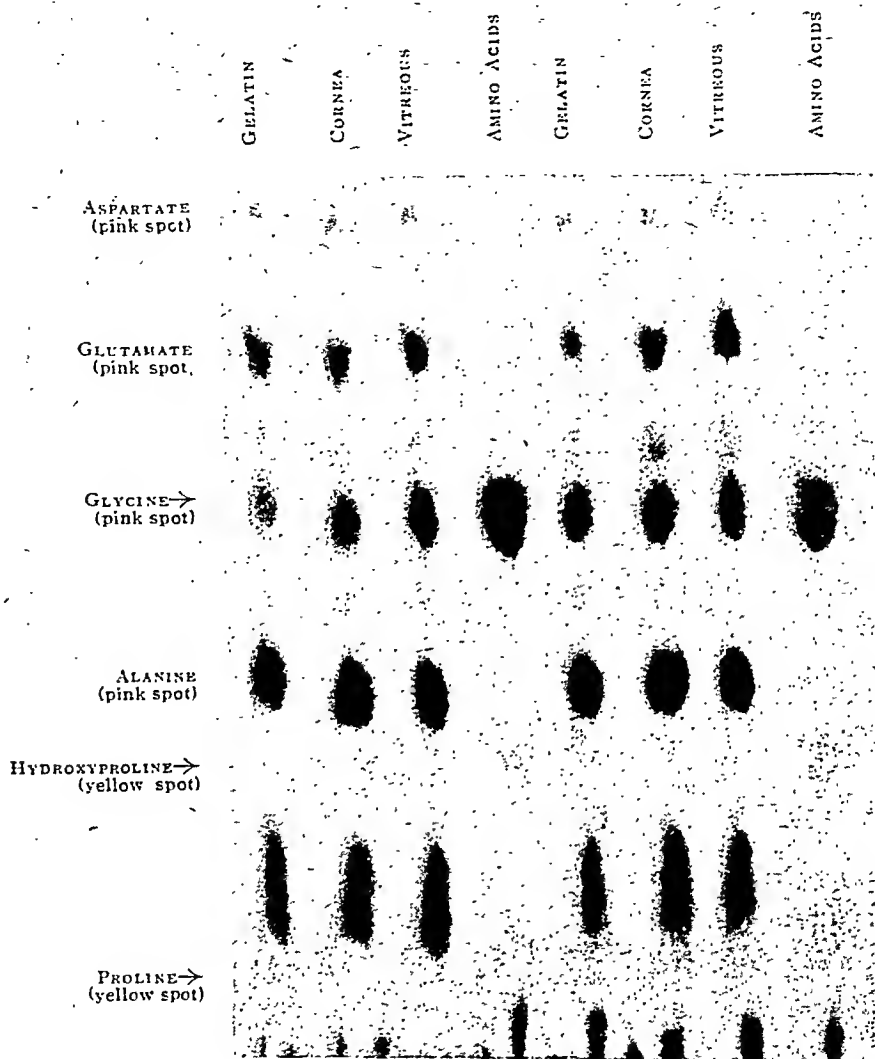


FIG. 1.

Partition chromatograms of hydrolysates of commercial gelatin, cornea gelatin, vitreous humour residual protein and a mixture of glycine, proline and hydroxy-proline. Whatman filter paper No. 1. Solvent saturated solution of phenol in water plus 0.7 per cent.  $\text{NH}_4\text{OH}$ .

the hydrolysates, but not in the others. While, therefore, there is no justification on the evidence of partition chromatography alone for identifying the nature and relative amounts of all the residues in the hydrolysates from the three sources, the evidence is sufficient to suggest that the vitreous humour protein might be a member of the collagen gelatin group.

## X-RAY ANALYSIS OF RESIDUAL PROTEIN

We have taken X-ray photographs of vitreous humour residues, both in the unstretched and the stretched state. Material was prepared for X-ray analysis by combined washing and filtration. Vitreous humours were suspended in saline and left in the ice chest for several days with frequent changes of saline. This preliminary washing removed most of the soluble protein and some hyaluronic acid. The humours were next suspended and washed in successive changes of distilled water in order to remove most of the salt, which would interfere with the X-ray photograph of the protein. The humours were then filtered by suspension on a glass filter and, after a further wash, the residue on the filter was dried. This residue, collected from several vitreous humours, was photographed without being stretched. In a further experiment and in order to get some orientation of the material, the vitreous humours were only partly filtered after being washed and while still wet were bunched together with a loop of cotton and hung on a clamp to drip further. When nearly all the contained fluid had dripped out, a loop of cotton was tied round the lower end of the bunch of humours and a 50 g. weight was attached. The bunch was now hung in a dessicator and allowed to dry completely while under tension. This dried material was always deep grey or black, probably owing to the presence of uveal pigment.

About 20 mg. of dry material, as prepared above, were compressed into a round specimen and photographed on a flat plate at a specimen-to-film distance of 4.0 cm. with an X-ray beam capable of recording up to 60 Å. A powder diagram was obtained whose spacings are recorded in Table I. The close resemblance of these spacings to the figures given by Astbury (1943) for collagen suggest that the protein of the vitreous humour can be classified as a collagen type.

Confirmation of this view has come from a study of stretched material prepared as already described. This method produced some degree of orientation, as was shown by the birefringence of the stretched residual protein which had been isotropic in the unstretched state. The X-ray photograph (Fig. 2), taken in this case on a cylindrical camera of radius 2.00 cm. and with the "fibre" axis of the specimen perpendicular to the X-ray beam, also demonstrates a considerable degree of orientation. The general agreement of the spacings of the X-ray reflections with those of oriented collagen fibres provides additional support for the view that the protein of the vitreous humour belongs to the collagen class.

TABLE I

SPACINGS GIVEN BY INSOLUBLE PROTEIN OF OX VITREOUS HUMOUR

<i>Spacings obtained from unstretched specimen</i>	<i>Spacings obtained from stretched specimen (calculated from Fig. 1)</i>	
	Equatorial	Meridian
A	A	A
2.9	2.1	2.9 (2.86; 2.91)
3.9	4.3 (4.4)	9.1 (9.5)
12.1	5.9 (5.62)	—
ca 50	11.8 (10.9)	—

The figures in brackets are those given by Astbury (l.c.) for collagen.

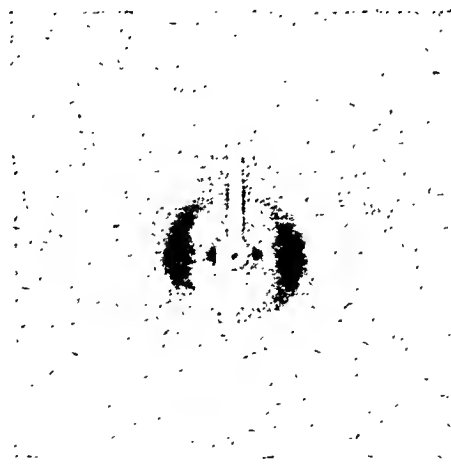


FIG. 2.

X-ray diagram of insoluble protein of ox vitreous humour. Stretched preparation showing orientation of fibres. Photograph taken with cylindrical camera, radius 3.00 cm. Cu radiation; Ni filtered.

#### ENZYME ANALYSIS OF VITREOUS RESIDUAL PROTEIN

The simplest test to find whether a given enzyme digests the residual protein of the vitreous humour is to see whether the enzyme takes the protein into solution. Previous workers have shown that the residual protein of the vitreous humour is, like collagen, dissolved by pepsin, but not by trypsin. We have confirmed this with our own preparations.

Through the kindness of Dr. W. E. van Heyningen we were able to test the effect of preparations of collagenase from *Cl. Welchii*. Bidwell and van Heyningen (1948) have shown that this enzyme digests only collagen and reticulin of all proteins so far tested, and this remarkable specificity makes it extremely useful for purposes of identification.

We found that a preparation of the enzyme readily dissolved the isolated residual protein of the vitreous humour. Small volumes of undiluted enzyme solution were next injected into the vitreous humour and Table II shows that collagenase preparations will liquefy the vitreous humour either in the eye or after extraction of the humour from the eye. Liquefaction was more complete after extraction, possibly because there was inevitable damage to the structure during removal from the eye, which made diffusion of the enzyme through the humour more rapid. After incubation with enzyme the vitreous humours were filtered and the residues on the filters—if any—were washed by suspension in water for some hours or days and were then dried *in vacuo* and weighed. In all experiments vitreous humours that had been injected with saline were used as controls.

TABLE II  
EFFECT OF *Cl. Welchii* COLLAGENASE ON OX VITREOUS HUMOUR

Experiment No.	Vitreous preparation	Enzyme addition ml.	Saline addition ml.	Time at 37° hr.	Gross effect	Weight of residue mg.
1	in ox eye	0.4	—	16	$\frac{1}{2}$ liquid	1.4
	"	—	0.4	"	intact	3.4
2	in ox eye	0.2	—	24	$\frac{1}{2}$ liquid	1.7
	"	—	0.4	"	intact	3.6
3	freshly extracted	0.4	0.2	20	liquid	none
	"	—	0.6	"	intact	3.6
4	after six days in saline	0.4	—	22	liquid	none
	"	—	0.4	"	intact	—
5	residue protein from filtered vitreous humour	0.1	0.9	24	dissolved	none

NOTE: *Cl. Welchii* collagenase preparation contained 220 Q enzyme units/ml. Eight ml. of enzyme preparation were mixed with 2 ml. antiserum containing 75 a units/ml., 70  $\phi$  units/ml. and 320 antihyaluronidase (Lister) units/ml. before use in these experiments.

The table shows that the collagenase preparation had an obvious liquefying effect on the vitreous humour and, in conjunction with this, the weight of insoluble residue remaining after filtration was smaller than in the controls. In some cases the residual protein was completely dissolved. The weights of the control residues were rather high, probably because they were only washed in water for a day or two before drying. We feared that prolonged washing would disintegrate the residues from the enzyme treated vitreous humours and so restricted the washing of all residues to short periods.

The evidence given by the various experimental methods described all suggests that the insoluble residue of the ox vitreous humour is largely made up of a protein of the collagen class. To the ophthalmologist, knowledge of the chemistry of the vitreous humour is mainly of interest if it increases knowledge of its development and of the normal and abnormal behaviour and appearance of the vitreous humour during life. The experiments reported here tell us nothing of the development of the vitreous humour, but we think that the results can be useful in formulating a more precise picture of the "meshwork of elastic fibrillae-suspended in a viscous fluid," which Robertson and Duke-Elder (l.c.) considered to be the structure of the vitreous humour, as a result of their work on its physical properties. In the following paragraphs we have, therefore, attempted an interpretation of the chemical results in terms of the behaviour of the vitreous humour under various conditions and we report experiments which we believe support this interpretation.

#### COMPARISON OF VITREOUS HUMOUR WITH COLLAGEN GEL

The insoluble protein in the vitreous humour appears to be laid down in a state of extremely fine division, either as a very fine meshwork of fibres or as extremely thin sheets. Such a network of molecular fineness is on the borderline of what is usually considered to be the structure of a gel.

We have, therefore, compared the properties of the vitreous humour with the properties of a collagen gel. Soluble collagen was first described by Nageotte (1927), who prepared it by treating rat tail tendon with very dilute acetic acid. Most of the tendon goes into solution and collagen may be re-precipitated either as macroscopic fibres, by neutralising the solution, or as a firm gel by dialysing the solution against distilled water to remove salts and acid. Nageotte and Guyon (1931) found that rat tail tendon collagen is the only collagen that goes into solution in this way. Tendons from the ox are insoluble.



We have prepared collagen gels of varying concentration from filtered solutions of rat tail tendon and have compared these with the vitreous humour. Gels in which the concentration of collagen is 0.3 per cent. or over do not break down when put on a filter, but gels of 0.07 per cent. or lower concentrations, could be filtered in exactly the same way as the vitreous humour, the collagen being left behind on the filter as a wisp-like residue. This collagen residue showed considerable anisotropy, particularly when stretched, rather like the residue from the vitreous humour and it stained brown with silver, again like the vitreous humour residue.

There were, however, two important differences between the gel residue and the vitreous humour residue. In the first place, the vitreous humour residue showed considerable tensile strength, even when wet, while the gel residue showed little or none. A more important difference was that when the gel residue was suspended in water it swelled and finally went completely into solution, whereas the vitreous humour residue showed no sign of dissolving under such conditions and remained intact for many months.

We consider, therefore, that the structure of the vitreous humour is rather different from a collagen gel, the differences between them perhaps showing that there is a firmer, more stable arrangement in the vitreous humour, which may perhaps be considered as a network of submicroscopic fibres. This picture, if correct, must conform with what is known of the properties of collagen and collagen fibres obtained from other sources.

#### SWELLING OF COLLAGEN AND SHRINKAGE OF VITREOUS HUMOUR

One of the most characteristic properties of collagen is its capacity to swell, the degree of swelling varying with the acidity or alkalinity of the solution. Fig. 3 gives the swelling curve of fresh, undried ox cornea collagen (Pirie, 1947) and shows that there is maximal swelling in acid, minimal at neutrality and intermediate swelling in alkaline solutions. Highberger (1939) has found that the isoelectric point of native skin collagen is pH 7.4-7.6, which corresponds with the zone of minimal swelling of cornea collagen.

If we apply these results to the vitreous humour we see that the fibres in it will be *minimally* swollen under normal conditions of neutrality, but will swell with any change, either towards acidity or alkalinity. This is exactly the reverse of the effect of acidity or alkalinity on the size of the vitreous humour as a whole. Many investigators have shown that there is very marked shrinkage of the vitreous humour in either acid or alkali and we found that the same is true for vitreous humour residues washed free from the

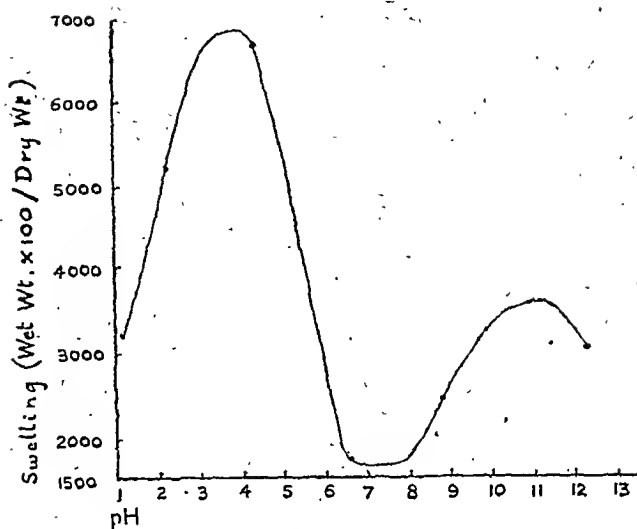


FIG. 3.

Swelling curve of ox cornea collagen.

soluble contents. A vitreous humour residue may have a wet weight of 10-15 g. at neutrality and one of 1-2 g. after suspen-

N

sion in — HCl.

100

We think that shrinkage of the vitreous humour and of the isolated vitreous humour residues in acid and alkali may be explained on the assumption that the fibres in it are arranged in a network. Küntzel (1926) showed that collagen fibres from rat tail shortened in length as they swelled in acid, the shortening being directly proportional to the degree of swelling of the fibre. This was confirmed by Jordan-Lloyd and Marriott (1935). If we consider a loose network of collagen fibres, swelling of these fibres will cause a shortening of each individual one. If the nodes are fixed, the shortening of each fibre will cause an over-all contraction of the whole structure because the lateral swelling of the fibres simply fills up the interfibrillar spaces which originally are very large compared to the volume of the fibres.

We suggest that the shrinkage of the vitreous humour in acid or alkali is due to the swelling and shortening of the fibres within it. Some evidence in favour of this view may be got from a study of the effect of salts on the volume changes in acid and alkali of the vitreous humour and of the isolated residues. Loeb (1920) showed that acid swelling of gelatin was depressed by salts, the degree of depression at any particular pH and salt concentration depending

upon the valency of the anion. Alkaline swelling of gelatin was also depressed by salts, the depression depending on the valency of the cation.

If salts act in this way on the fibres of the vitreous humour we should expect that the volume of the vitreous humour, which we suggest is *inversely* related to the volume, or degree of swelling of the fibres within it, will be greater in acid plus salts than in acid alone. We should also expect that salts with di- or tri-valent anions will be more effective in reducing the shrinkage of the vitreous humour in acid than salts with monovalent anions.

A great deal of work on swelling and shrinkage of vitreous humour has already been done, in some of which the effect of salts was examined. A difficulty in assessing these results is that the fresh vitreous humour contains both soluble and insoluble constituents and when suspended in acid or alkali the soluble constituents—if not precipitated—will diffuse into the surrounding fluid, thus altering its composition. The amount of salts diffusing out of the humour may appreciably change the concentration in the solution unless the volume of solution is very great or it is renewed after some time.

#### EFFECT OF SALTS ON VOLUME OF WASHED VITREOUS HUMOUR RESIDUES

We have examined the effect of salts on acid and alkaline swelling of the washed vitreous humour residues. By using such washed residues we have avoided any complication due to precipitation of vitreous mucin by acid, and lack of equilibrium owing to outward diffusion of soluble constituents, including salts. The results we obtained were the same as those for fresh vitreous humours, but we found that the final volume was much more rapidly obtained and, in general, the valency effect was more clearly shown.

Each washed residue or fresh vitreous humour was put in a stoppered flask containing 200 ml. of the appropriate solution and left on the bench for 24-48 hours. The volume of the vitreous residue or fresh vitreous humour was determined both before and after suspension in fluid by placing in a measuring cylinder of appropriate size and reading off the volume. The pH of the solutions was determined electrometrically before and after immersion of the vitreous preparations in them.

Table III shows the percentage decrease in volume of washed vitreous residues after immersion in different salt solutions at either acid or alkaline pH. The first experiment shows that in acid the monovalent anion  $\text{Cl}^-$  has practically no effect on vitreous shrinkage, the divalent anion  $\text{SO}_4^{--}$  diminishes vitreous shrinkage considerably and the trivalent anion  $\text{Fe}(\text{CN})_6^{--}$  in a much lower concentration almost abolishes the shrinkage. Experiment two shows

TABLE III

EFFECT OF SALTS ON ACID AND ALKALINE SHRINKAGE OF WASHED VITREOUS HUMOUR RESIDUES

		HCl at pH 2.0					
Expt.	Salt added	None	$\frac{M}{128}$ NaCl	$\frac{M}{128}$ Na <sub>2</sub> SO <sub>4</sub>	$\frac{M}{1024}$ K <sub>3</sub> Fe(CN) <sub>6</sub>		
1	Per cent. decrease in volume	82	79	36	14		
		HCl at pH 1.8					
	Salt added	None	$\frac{M}{64}$ CaCl <sub>2</sub>	$\frac{M}{64}$ AlCl <sub>3</sub>	$\frac{M}{64}$ K <sub>2</sub> SO <sub>4</sub>	$\frac{M}{1024}$ K <sub>2</sub> SO <sub>4</sub>	$\frac{M}{1024}$ K <sub>3</sub> Fe(CN) <sub>6</sub>
2	Per cent. decrease in volume	94	92	92	50	85	30
		NaOH at pH 11.1					
	Salt added	None	$\frac{M}{512}$ NaCl	$\frac{M}{512}$ CaCl <sub>2</sub>			
3	Per cent. change in volume	-78	-63	+18			
		NaOH at pH 11.4					
	Salt added	None	$\frac{M}{256}$ KCl	$\frac{M}{256}$ K <sub>2</sub> SO <sub>4</sub>	$\frac{M}{256}$ CaCl <sub>2</sub>	$\frac{M}{32}$ K <sub>2</sub> SO <sub>4</sub>	
4	Per cent. decrease in volume	61	77	56	23	36	

that calcium chloride and aluminium chloride do not depress shrinkage in acid, which is in favour of the view that this effect in acid is dependent on the valency of the anion not the cation. It

also shows that although  $\frac{M}{64}$  K<sub>2</sub>SO<sub>4</sub> depresses shrinkage,  $\frac{M}{1024}$

has little effect, while  $\frac{M}{1024}$  K<sub>3</sub>Fe(CN)<sub>6</sub>, a salt with a trivalent anion,

has a greater effect than  $\frac{M}{64}$  K<sub>2</sub>SO<sub>4</sub>. Experiments three and four

show that in alkali CaCl<sub>2</sub> reduces shrinkage—in fact, in one case there is slight expansion—while KCl and NaCl have no effect. In

alkali, therefore, shrinkage is depressed according to the valency of the cation of the added salt.

We found that if those vitreous residues which had been immersed in  $K_3Fe(CN)_6$  or  $K_2SO_4$  solutions were washed free of salts and then put in HCl of pH2 they shrank further until they equalled in size the vitreous residues that had been placed directly in acid. This shows that the salts that depress vitreous shrinkage have no permanent effect. The dry weight of fully shrunken residues whose volume was between 1-2 ml. was the same as the dry weight of vitreous residues held at neutrality, showing that the shrinkage was not due to solution of the residue by the acid.

These experiments were repeated using fresh vitreous humours. We found that one ox vitreous humour could change the pH of 200 ml. dilute acid or alkali by as much as two units and it was necessary to transfer the humours to fresh solutions after 24 hours, both in order to obtain the required pH and also to dilute the salts which had diffused out of the vitreous itself.

TABLE IV

EFFECT OF SALTS ON ACID AND ALKALINE SHRINKAGE OF FRESH VITREOUS HUMOUR

Expt.	Salt	HCl at pH 2.2			
		None	$\frac{M}{128}$ NaCl	$\frac{M}{128}$ $K_2SO_4$	$\frac{M}{1024}$ $K_3Fe(CN)_6$
1	per cent. decrease in volume	71	76	62	26
2	Salt	NaOH at pH 11.2			
		None	$\frac{M}{256}$ KCl	$\frac{M}{256}$ $CaCl_2$	$\frac{M}{32}$ KCl $\frac{M}{32}$ $CaCl_2$
	per cent. decrease in volume	70	62	8	52 8

The shrinkage of fresh vitreous humour in acid or in alkali was also depressed by the addition of salts, in acid the depression was related to the valency of the anion and in alkali to the valency of

the cation. Table V shows that  $\frac{M}{4}$  KCl has about the same effect as

$\frac{M}{32}$   $K_2SO_4$  or  $\frac{M}{1024}$   $K_3Fe(CN)_6$ .

TABLE V

EFFECT OF DIFFERENT CONCENTRATIONS OF  $KCl$ ,  $K_2SO_4$  AND  $K_3Fe(CN)_6$  ON VOLUME OF FRESH VITREOUS HUMOUR IN  $HCl$  AT pH 1.8

Molarity of salt	Final volume of vitreous humour ml.		
	$KCl$	$K_2SO_4$	$K_3Fe(CN)_6$
0	1.5	1.5	1.5
$\frac{M}{4}$	8.0	—	—
$\frac{M}{32}$	5.0	8.0	—
$\frac{M}{64}$	—	5.0	—
$\frac{M}{128}$	2.5	2.5	—
$\frac{M}{512}$	3.5	3.0	—
$\frac{M}{1024}$	3.5	4.0	7.5

All vitreous humours had an initial volume of 14—15 ml. The final volumes were measured after 64 hours. The humours were transferred to fresh solutions after 24 hours, to avoid effect of salts diffusing from vitreous itself.

Salts, therefore, depress *shrinkage* of the vitreous humour, just as Loeb (l.c.) found they depressed *swelling* of gelatin. We think it is most likely that they are having the same effect in both cases, depressing the acid and alkaline swelling of a protein. The results support the view that the insoluble vitreous residual protein is laid down as a meshwork of fibres, each of which will swell and shorten in acid or alkali and so cause shrinkage of the whole vitreous humour.

### Discussion

Slit-lamp examination of the vitreous humour during life or after extraction shows that it is not optically empty, but that it may contain sheets or membranes of reflecting material. Friedenwald

and Stiehler (1935), using the slit ultra-microscope to examine the extracted vitreous-humour of the ox, observed fairly regular bright reflections which they interpreted as due to very thin sheets of the residual protein. The bright reflections ran roughly parallel to the surface of the vitreous humour and were separated from one another by spaces of 0.5-3 microns. Friedenwald and Stiehler considered that the thickness of the sheets was of the same order of magnitude as the wave length of light and they thought that the cohesion between sheets might form the visible opacities of the degenerating humour. Vogt (1941), who has studied the vitreous humour in the living human eye, speaks of the scaffolding of the vitreous body and states that it is predominantly lamellar in structure, that is, membranous, but that a fibrillar structure in the membranes can often be made out. Vogt's very beautiful pictures of vitreous opacities fit with the idea that these are formed by cohesion between membranes or fibres.

The vitreous humour of the ox appears to be a more rigid structure than that of any other animal so far examined. Meyer, Smyth and Gallardo (1938) have found that ox vitreous humour contains a great deal more hexosamine than the humours of other animals. This indicates that the hyaluronic acid content of ox vitreous humour is greater and probably explains its greater rigidity. In spite of such quantitative differences between animals, there appears to be a qualitative similarity, both in the slit-lamp appearance and in the chemistry of the vitreous humours of different species.

If the experimental evidence given here is accepted the picture of the structure of the vitreous humour becomes more complex. It cannot be considered as uniform, but must be made up of at least two "structures," the collagen-like network and the hyaluronic acid and protein jelly. Liquefaction of the humour follows enzymic hydrolysis of the network and therefore one may say that this network is essential for maintenance of a normal vitreous humour. Yet it does not form the humour, being minimally swollen at neutrality and occupying only a very small part of the total volume. It seems to us that it is the relation of the network to the jelly which is of first importance and must be taken into account in any theories of the causes of vitreous swelling and vitreous degenerations.

#### SUMMARY

1. X-ray photography, amino acid chromatography and enzyme analysis provide evidence that the residual protein of the ox vitreous humour is largely a collagen type.

2. Enzyme preparations containing collagenase liquefy the ox vitreous humour.

3. The bearing of this result on the conception of vitreous humour structure is discussed.

We are deeply indebted to Dr. D. S. Parsons and Dr. R. B. Fisher for carrying out the amino-acid partition chromatograms on our material and for their interpretation of them. We also wish to thank Mr. Tugwell, photographer to the Radcliffe Infirmary, for the care he has taken in preparing the photographs of the chromatograms.

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## VARIATION OF PUPIL SIZE WITH CHANGE IN THE ANGLE AT WHICH THE LIGHT STIMULUS STRIKES THE RETINA\*

BY

K. H. SPRING and W. S. STILES

THE possibility of a variation in pupil size depending on the part of the natural pupil through which the light from the external field enters the eye has not been examined hitherto. Such a variation might occur for two reasons: (a) since the apparent brightness of an illuminated field is reduced if the rays enter near the edge rather than near the centre of the pupil (directional sensitivity of the retina†), a slightly larger pupil might be expected in the former case; (b) if, as is possible, the protective action of the constricted pupil consists not so much in reducing the total light flux as in excluding rays which would otherwise strike the retina obliquely; such rays might prove more effective in closing the pupil than rays incident normally. The pupil would then be smaller for rays entering near the edge. While variations from these causes are likely to be smaller than the effects of changes in field brightness and field area, they would be of considerable theoretical interest and would have a bearing on the efficient design and use of optical instruments. In the present work, carried out at the request of the Director of Scientific Research, Admiralty, measurements of the pupil were made under conditions specially arranged to reveal any change of size with change in the point of entry of the light in the pupil.

To obtain the greatest possible separation between rays entering centrally and near the edge, the pupil must be fully dilated. On the other hand it is the pupil of moderate size which is most sensitive to changes in the conditions of illumination. Both requirements were met by exposing the illuminated field to one eye only, the pupil of this eye being kept fully dilated with a mydriatic, and by determining by flash photography the variations in size of the free (unmydriatised) pupil of the other eye which was kept in the dark. It was confirmed that a given light stimulus entering either eye affected both pupils about equally and that mydriasis of one pupil did not interfere with the reaction of the other.

In the two sets of main measurements, made on 12 subjects, the

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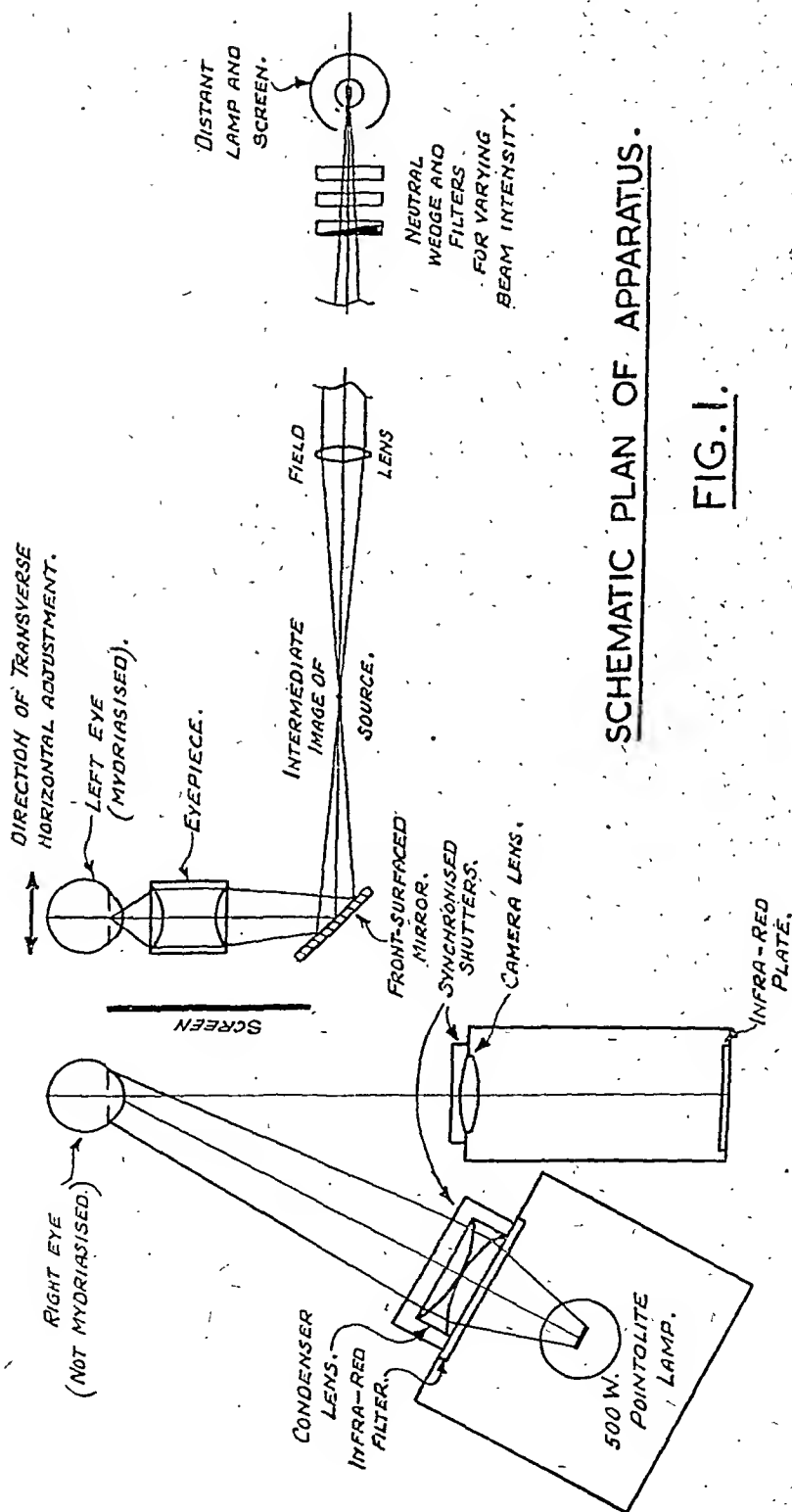
† For a review of the work done up to 1939 on this property of the retina (Stiles-Crawford effect) see Stiles, *Science Progress*, Vol. XXXIII, p. 176, 1939.

rays from a Maxwellian field of  $52^\circ$  diameter (white light) were focused in the plane of the mydriatised pupil of the left eye, the cross-section of the beam in this plane being approximately 0.5 mm. Thus the free right pupil was the one photographed. The principle of the apparatus is made clear by the sketch in Fig. 1 (not to scale). The subject's head was kept rigid by requiring him to bite on a dental impression which was clamped to a massive lathe slide-rest mounted on the table carrying the optical apparatus. The 3-dimensional adjustment of the slide-rest enabled the subject's eyes to be brought into precisely the correct position with respect to the apparatus. Also by means of the transverse horizontal adjustment the head could be moved so that the rays from the  $52^\circ$  field entered the dilated pupil of the left eye at any point on a horizontal diameter. For photographing the right pupil, the infra-red light from a 500 watt Pointolite was focused on the eye and exposed by a shutter for  $1/20$ th sec. A second, synchronised shutter exposed the camera lens. Kodak Extra-Rapid Infra-red plates were used.

In the first series of main measurements the beam entered the left eye centrally. The variation of the apparent pupil size (apparent horizontal diameter) of the right eye was determined for field intensities from zero to  $10^5$  luxons (photons)\*. The results for the 12 subjects (average age 29, range 25-46) are shown in Fig. 2, each curve being based on 2 or 3 sets of measurements. In each set, the observations began after the subject had been in the dark for about 15 min. Thereafter, the right pupil was photographed after 3 min. exposure of the left eye to each of an increasing series of field brightnesses. The left pupil was not mydriatised. There are very large individual differences and it may be noted that for several subjects the decrease in pupil size with increase in field brightness appears to occur in two stages. The results of these subjects are chiefly responsible for the slight irregularity in the mean curve (Fig. 3) at an intensity in the neighbourhood of  $10^{0.5}$  luxons (marked X). The second curve in Fig. 3 gives the mean results obtained in an unpublished investigation by the Admiralty Research Laboratory in which the subjects (52, average age 24) viewed, binocularly and with the natural pupil, a field of  $50^\circ$  diameter. This curve also shows a slight irregularity (marked Y) but at a much lower intensity,  $10^{-0.9}$  luxons.

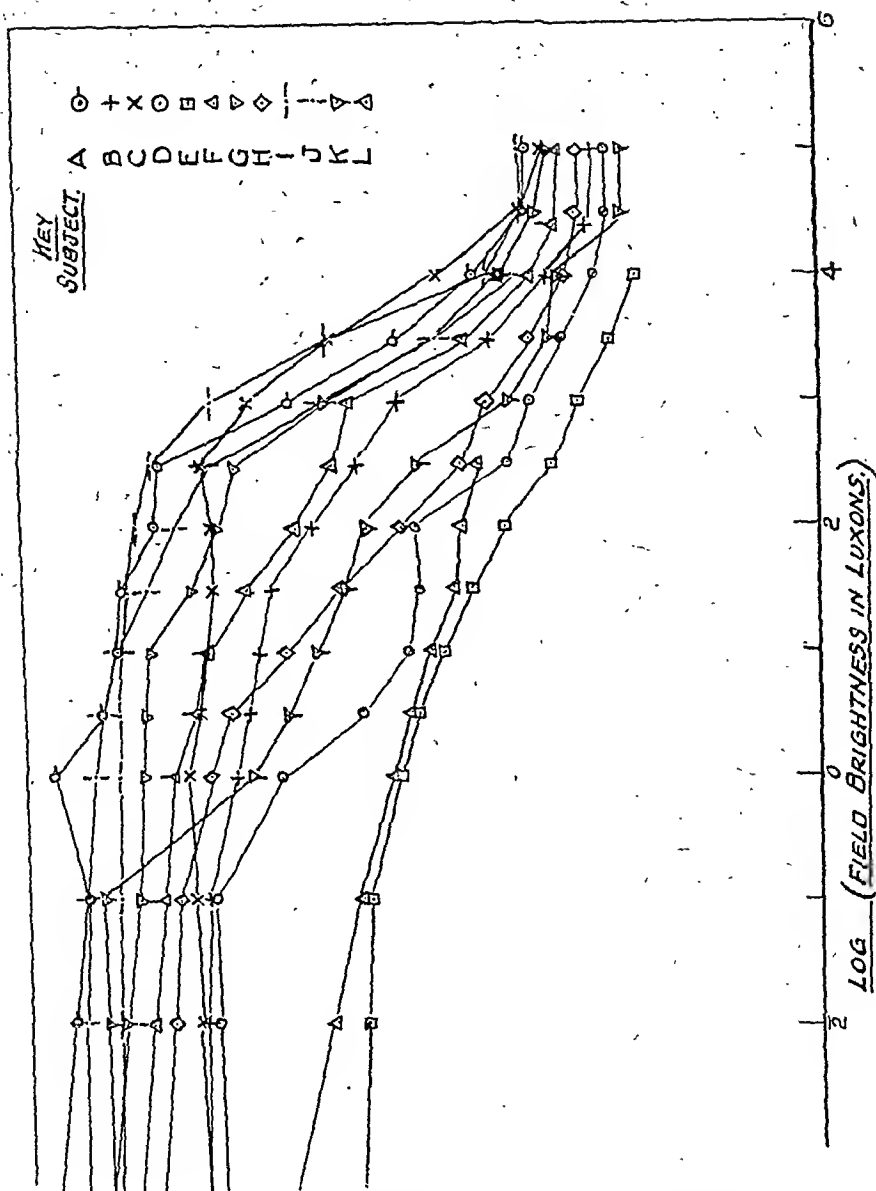
To investigate the variation of apparent pupil size with point of entry a fixed field brightness in the range indicated in Fig. 3 was used. The left pupil was mydriatised, and the right photographed

\* The photon is a unit of retinal illumination, and is the illumination corresponding to an external field of brightness one candle per square metre seen through a pupil of 1 sq. mm. area. Following Blottiau, the term "luxon" is now used to avoid confusion with the "photon" of quantum theory.



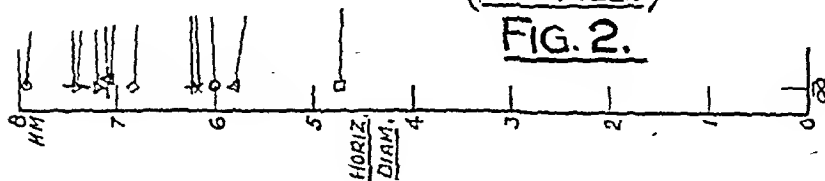
SCHEMATIC PLAN OF APPARATUS.

FIG. 1.



PUPIL SIZE - FIELD BRIGHTNESS  
CURVES FOR 12 SUBJECTS  
(52° FIELD.)

FIG. 2.



after the usual 3 minute preadaptation. The individual results (Fig. 4) are the means derived from 3 or 4 traverses of the pupil. A few of the more regular graphs show a tendency for the pupil to dilate slightly for eccentric entry. For the mean curve (Fig. 5) the change is very small and may not be significant: there is an increase from a diameter of 3.75 mm. for central entry to 4.1 mm. for entry at 3 mm. nasal and 4.0 mm. for entry at 3 mm. temporal.

As the point of entry is traversed across the pupil the apparent brightness of the field changes. For foveal vision, the apparent brightness is reduced by a factor  $\eta$ , given approximately by the formula  $\log \eta = -0.05d^2$  where  $d$  is the distance of the point of entry from the pupil centre, expressed in mm. (Stiles, 1939). Taking for each subject the gradient of the curve of pupil diameter against  $\log$  (field brightness) (Fig. 2), at the brightness used for the traverse measurements (Fig. 4), the change of pupil size with position of the point of entry can be calculated, on the assumption that it arises solely from the change in apparent field brightness predicted by the above formula. The mean curve calculated in this way is shown in Fig. 5. It is evident that the observed variation is less than that calculated. The calculation assumes in effect that at the brightness levels in question only the retinal cones are concerned in determining the pupil size. The retinal rods have nearly the same sensitivity for all points of entry of a light stimulus and if they are participating in the control of the pupil the variation of pupil size with point of entry may be expected to be less.

Comparison for each subject of the pupil size obtained in the traverse measurements (Fig. 4) with the pupil size at the same brightness in the brightness level measurements (Fig. 2) shows that the mydriasis of the left pupil in the former case has not affected the control of the right pupil by the light stimulus entering the left eye. The difference in pupil size for the two cases averaged over the 12 subjects is 0.13 mm.

It may be concluded from the present measurements (a) that rays entering near the edge of the dilated pupil, and hence incident on the retina at an angle with the normal, produce no abnormally high pupillomotor effect and (b) that for practical purposes the part of the pupil through which light enters the eye is not a factor in determining pupil size.

*Acknowledgment.* The work described above was carried out in the Light Division of the National Physical Laboratory on behalf of the Chief of the Royal Naval Scientific Service, by whose permission this paper is published.

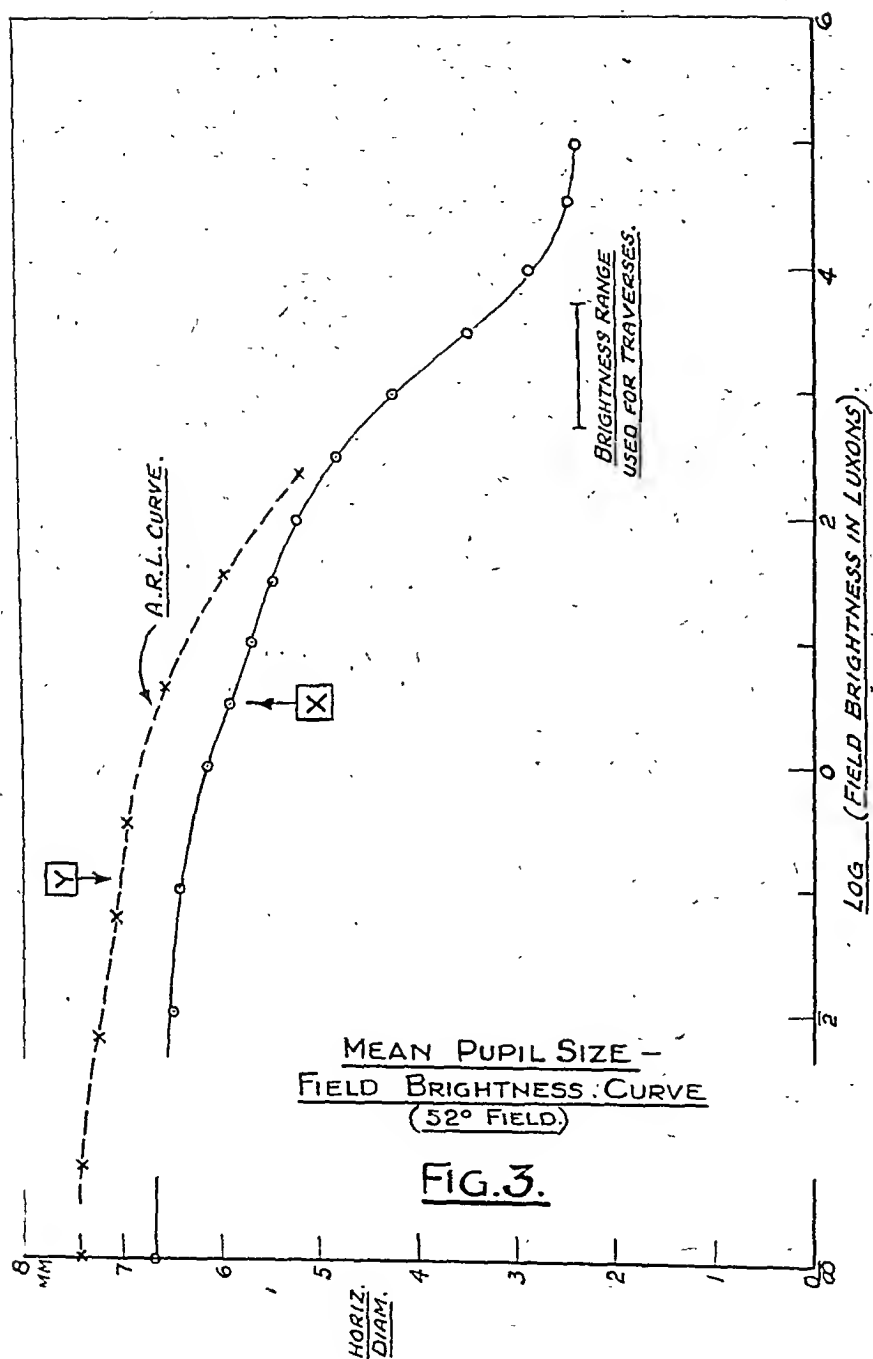
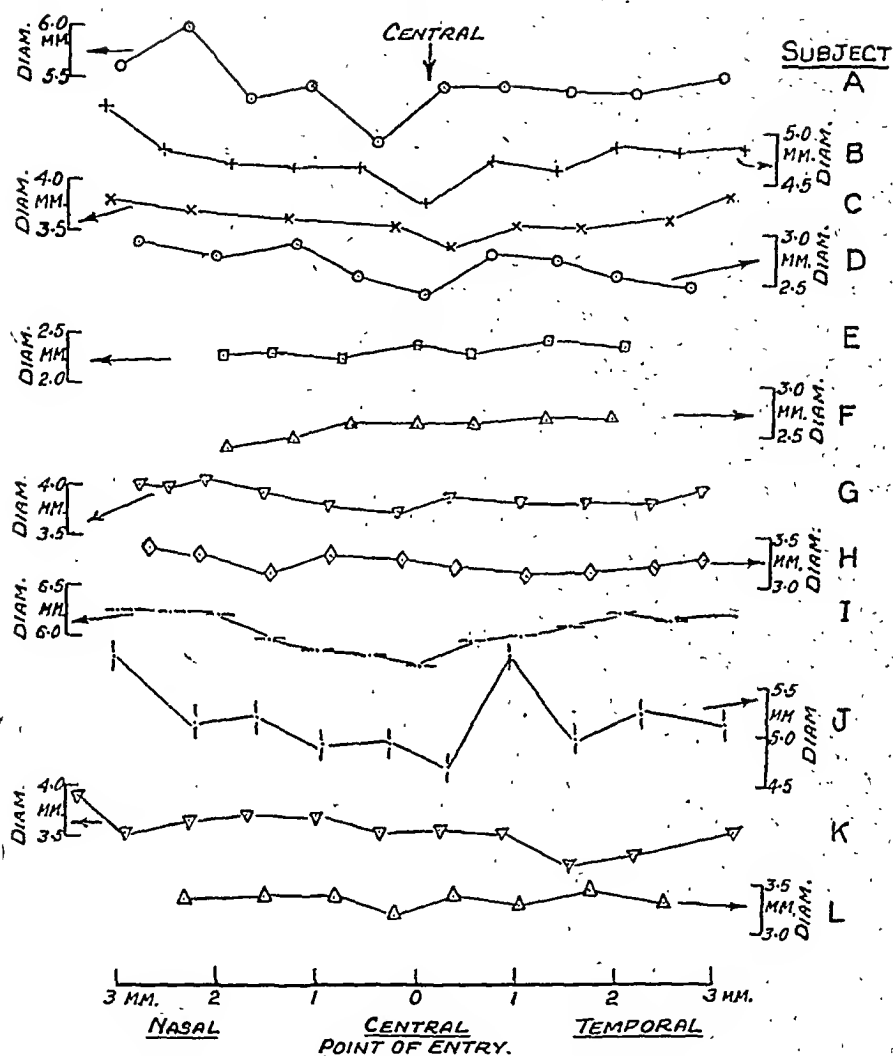
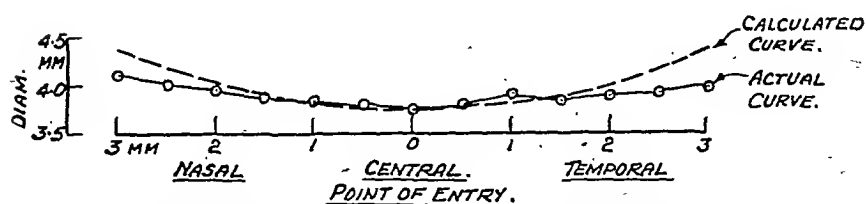


FIG. 3.



TRAVERSES FOR 12 SUBJECTS (52° FIELD)

FIG. 4.



CALCULATED, AND MEAN EXPERIMENTAL, CURVES.

FIG. 5.

APPARENT SHAPE AND SIZE OF THE  
PUPIL VIEWED OBLIQUELY\*

BY

K. H. SPRING *and* W. S. STILES

IN studies of the response of the peripheral retina, a knowledge of the apparent shape and size of the pupil for large angles of view is sometimes necessary. By photographing the pupil at various angles in the horizontal meridian from  $20^\circ$  nasal to  $105^\circ$  temporal the mean results shown in Table I were obtained for a group of 13 subjects. In the case of the large pupil, the pupil was fully dilated with a mydriatic and the field of view was kept dark until the light-flash for the exposure was given. These results refer therefore to a pupil whose actual size may be taken as constant for all angles of view. The variations of apparent size are attributable solely to the obliquity and to the refraction of the cornea and aqueous. For the small pupil results on the other hand the pupil was free, *i.e.*, no miotic was used, but it was kept small by being permanently exposed to the light source used for the photography. In these circumstances the actual pupil size could not be taken as constant for the various exposures and, for this reason, only the ratio of horizontal and vertical diameters determining the approximate shape of the apparent pupil is reported. The individual variations in shape for both large and small pupils are shown by the plots of this ratio in Figs. 1 and 2.

In view of the angular displacement of the optic axis relative to the visual axis, the mean curves of Figs. 1 and 2 may be expected to be symmetrical about an ordinate at about  $5^\circ$  temporal. As far as can be judged with only one observational angle on the nasal side, this is the case. It will be noted (column 3 of Table I) that for the large pupil the apparent vertical diameter varies little with angle but shows a maximum at about  $80^\circ$  temporal.

For a simplified eye consisting of a refracting sphere of index 1.336 and radius 7.8 mm. in which the pupil is imbedded at a distance 3.3 mm. from the "corneal" surface, the calculated apparent areas for various angles of view and for large and small pupils are shown in Fig. 3. The area for observation along the optic axis is taken as unity and allowance is made for a  $5^\circ$  separation of the optic and visual axes. The mean experimental curve for the large pupil is shown in the same diagram as well as the

\* Communicated by the National Physical Laboratory. Received for publication April 15, 1948.



simple cosine curve which would be obtained if there were no corneal refraction. It is apparent that the calculated values deviate materially from the observed values for angles of view exceeding about  $70^\circ$ .

Good sets of pupil photographs at different angles are reproduced in Figs. 4 and 5. For these, the pupil has a non-zero and fairly well defined area at  $105^\circ$ , the largest angle used. In many cases the interpretation of the large angle photographs is difficult, particularly for brown (pigmented) eyes, where contrast between iris and pupil is low. In the example of Fig. 4 the far edge of the pupil approaches the corneal surface at  $70^\circ$  to  $80^\circ$  angle of view but subsequently recedes. Qualitatively, this is what would be expected from the simple theory mentioned above. There is considerable individual variation in the apparent position of the pupil at oblique angles of view.

If it is assumed that the apparent vertical diameter of the small pupil, like that of the large pupil, varies little with angle the average apparent area for pupils of any size and angle of view can be estimated approximately by interpolation. This is done in Table II, which assumes (1) that the relative apparent vertical diameters at different angles are the same for all pupil sizes and correspond to the values for the large pupil given in column 3 of Table I, (2) that, at a given angle, the ratio of horizontal to vertical diameters may be taken as a linear function of the apparent pupil diameter for normal view, *i.e.*, linear interpolation between columns 4 and 6 of Table II can be applied, (3) that the eye may be taken as a system symmetrical about an axis (the optic axis) inclined  $5^\circ$  to the temporal side of the visual axis.

*Acknowledgment.* The work described above was carried out in the Light Division of the National Physical Laboratory on behalf of the Chief of the Royal Naval Scientific Service, by whose permission this paper is published.

TABLE I

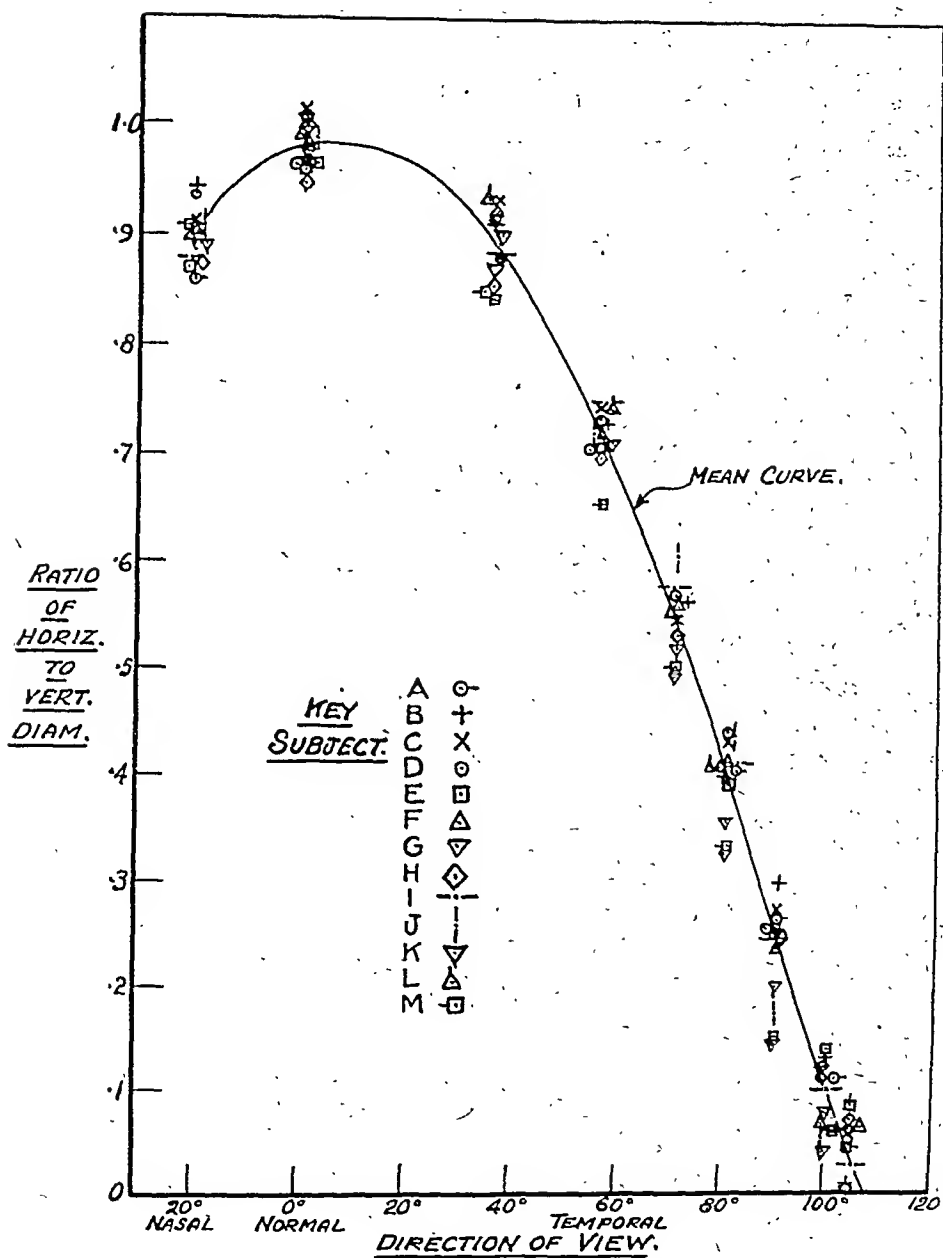
Direction of view of the camera with respect to the visual axis	Large pupil				Small pupil*
	Mean Appt. Hor. Diam.	Mean Appt. Vert. Diam.	Ratio of Hor./Vert. Diam.	Appt. Area	Ratio of Hor./Vert. Diam.
20° Nasal	7.13 mm.	7.94 mm.	0.90	44.4 mm. <sup>2</sup>	0.91
0°	7.69	7.84	0.98	47.3	1.00
35° Temp.	7.01	7.83	0.90	43.1	0.90
55° Temp.	5.72	7.99	0.72	35.9	0.73
70° Temp.	4.43	8.15	0.54	28.3	0.53
80° Temp.	3.25	8.19	0.40	20.9	0.40
90° Temp.	1.18	8.15	0.23	12.0	0.28
100° Temp.	0.75	7.72	0.10	4.5 <sub>3</sub>	0.15
105° Temp.	0.25	7.44	0.03	1.4 <sub>6</sub>	0.07

\* Mean apparent vertical diameter at 0° = 2.66 mm.

TABLE II

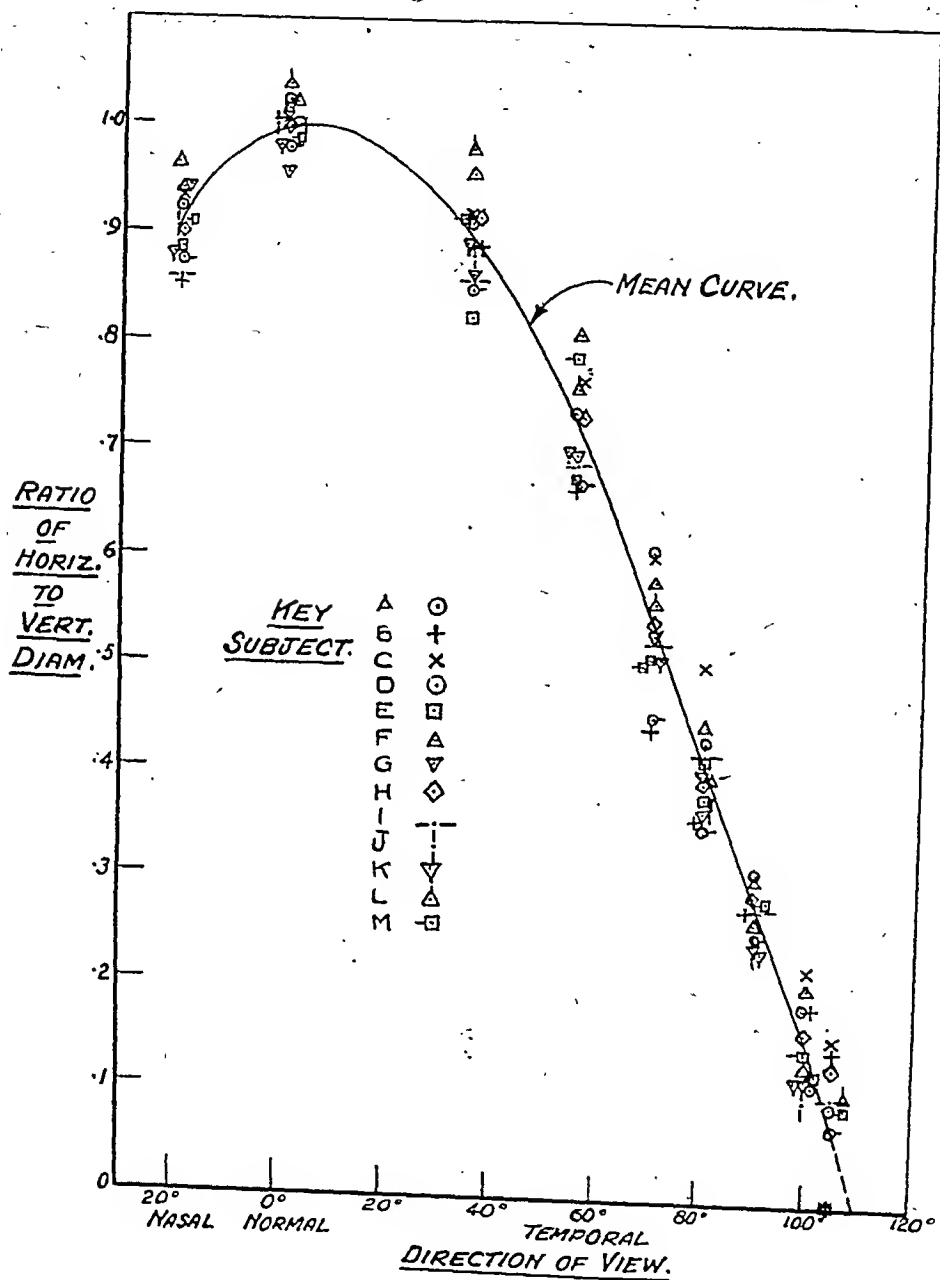
Factor by which the area of the apparent pupil is reduced for objects in the peripheral field. Area for an object on the visual axis taken as unity.

Angle between direction of object and the optic axis of the eye	Apparent pupil diam. for object on the visual axis			
	8 mm.	6	4	2
5° (corresponding for example to object on visual axis)	1.00	Factor 1.00	1.00	1.00
25	0.94	0.94	0.94	0.94
50	0.76	0.76	0.76	0.76
75	0.44	0.44	0.44	0.44
85	0.25	0.27	0.29	0.30
95	0.094	0.114	0.132	0.150
100	0.030	0.042	0.053	0.064



VARIATION OF PUPIL SHAPE WITH  
OBLIQUITY—LARGE PUPIL.

FIG. I.



VARIATION OF PUPIL SHAPE WITH  
OBLIQUITY-SMALL PUPIL.

FIG. 2.

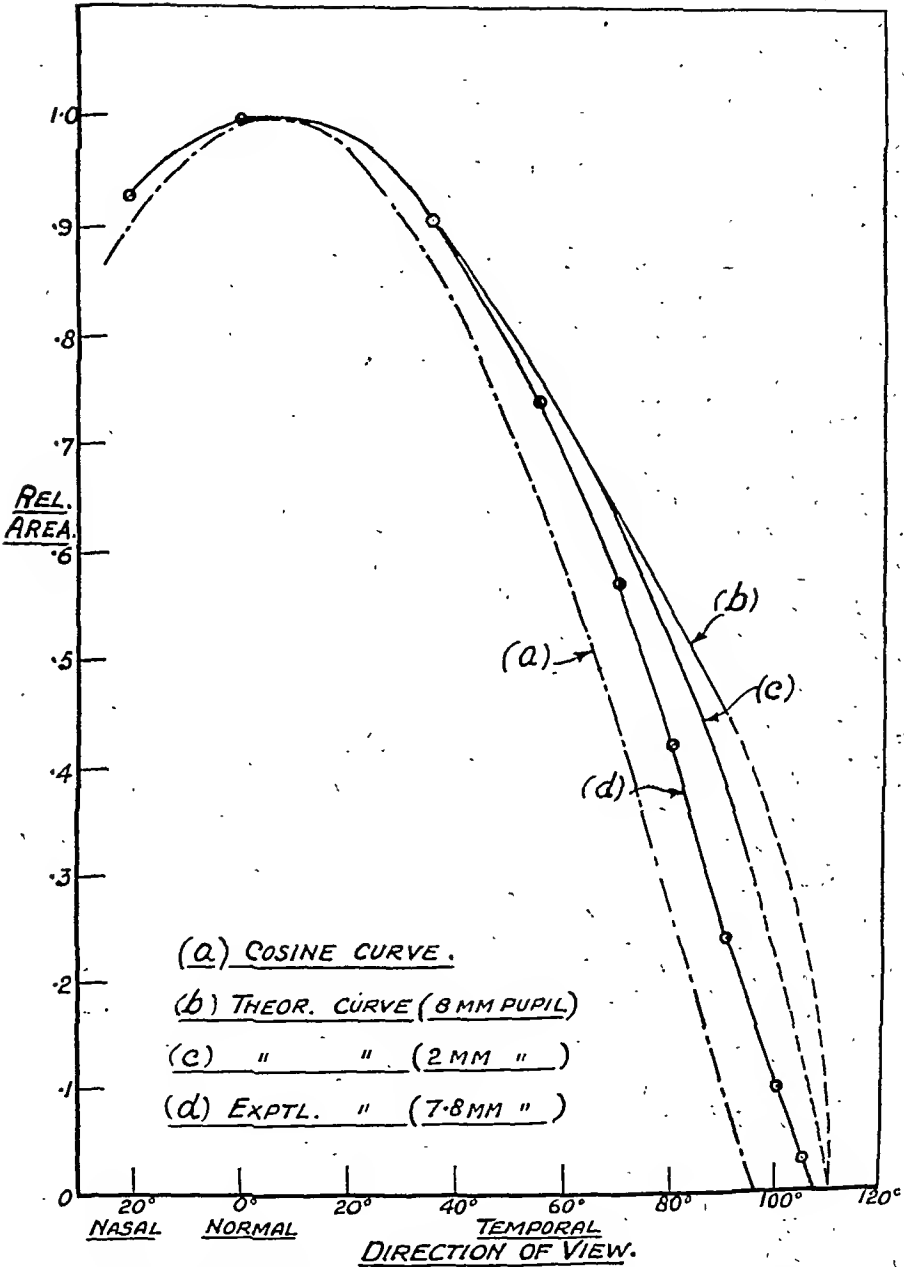
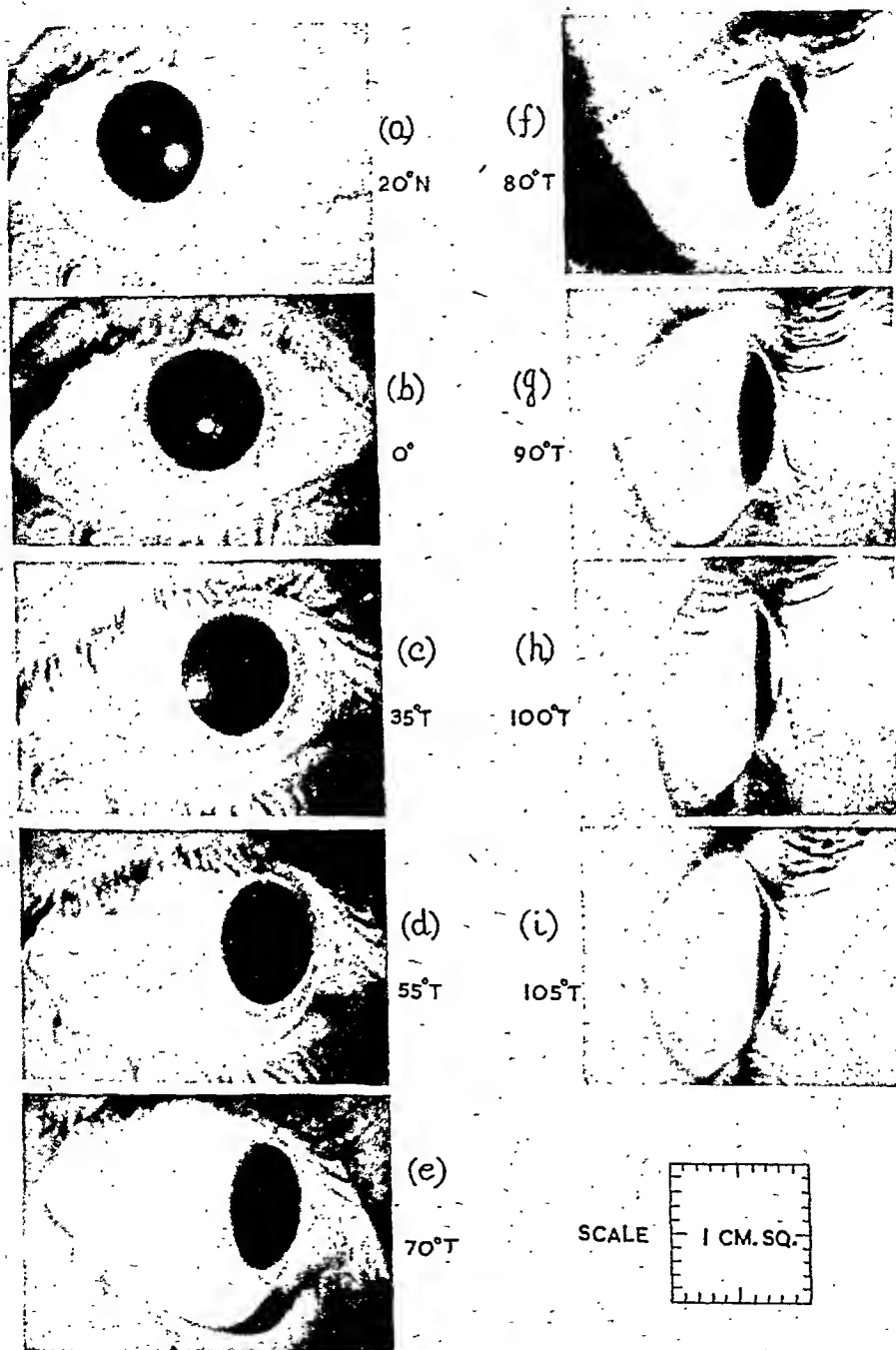
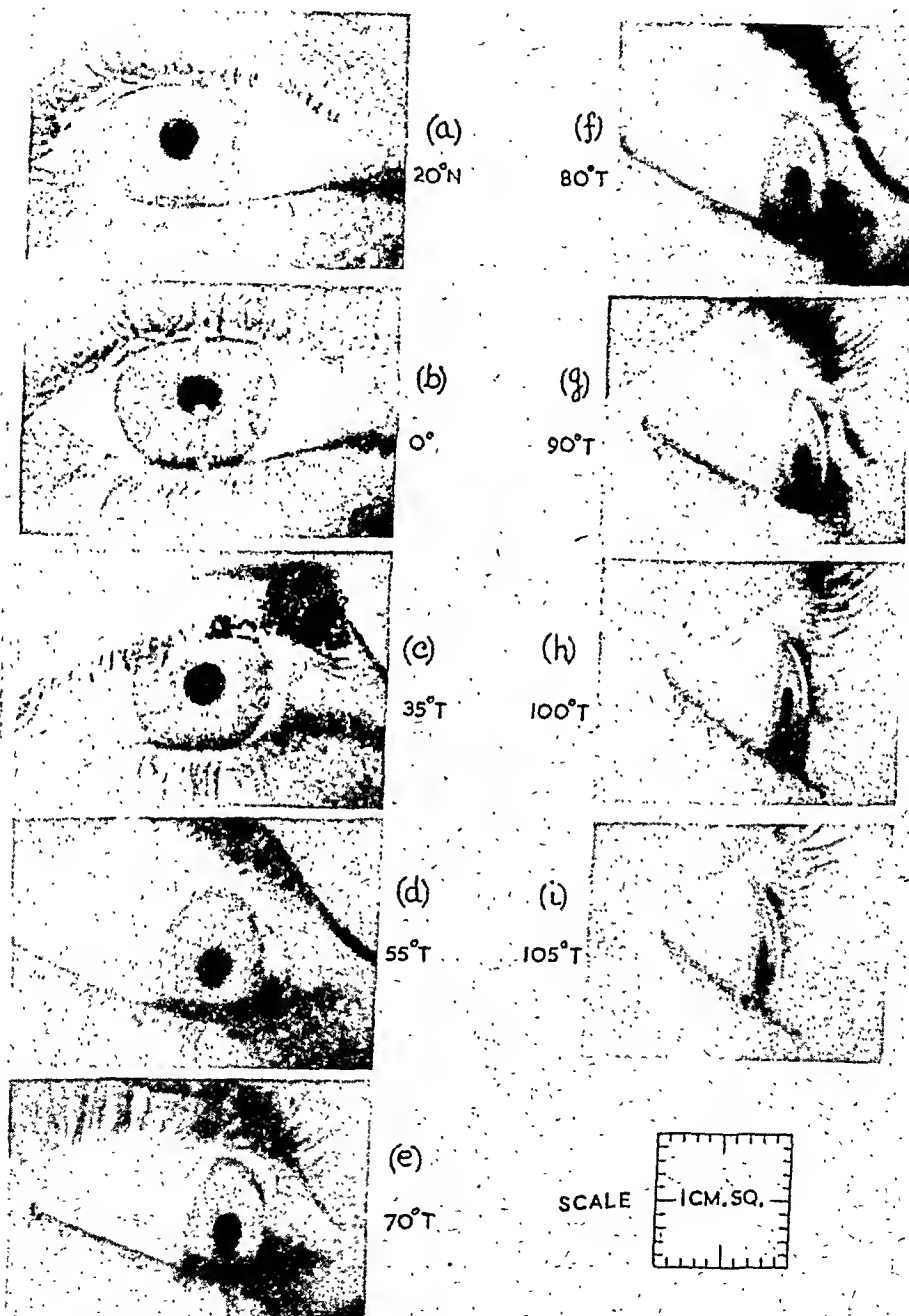


FIG.3.



LARGE (DILATED) PUPIL VIEWED AT DIFFERENT  
OBLIQUITIES. SUBJECT 'A'.



SMALL PUPIL VIEWED AT DIFFERENT  
OBLIQUITIES. SUBJECT "C."

## THE ALTERATION IN SIZE OF THE NORMAL OPTIC DISC CUP \*

BY

RANSOM PICKARD

EXETER

IN 1920 a paper (a) was read by me before the Ophthalmic Section of the Royal Society of Medicine in which it was deduced, from the sizes of the optic disc cups at different ages; that the cup normally increased in size with age. In another paper, read before the South Western Ophthalmological Society in 1935 (b) at Bath, a diagram was exhibited showing increases actually observed. In the present paper 234 eyes, observed for a period of fifteen years or nearly so will be compared with 280 eyes, observed contemporaneously with the fifteen year group, but observed only once, and not included in that group. Finally these two groups are combined together, and a general rule as to the average growth deduced.

All the discs recorded were normal in appearance. Cases of cataract were included if the discs were sufficiently clear to be drawn. Similarly small corneal nebulae were included. All other forms of disease in the eyes were excluded. There were no cases of abnormal congenital conditions in these series.

The method of recording was that devised by me in 1920 and practised by me since then. The outline of the disc is drawn of its apparent size. The outline of the cup at the surface of the disc is then drawn of its apparent size and in its proper position. Similarly the outline of the bottom of the cup is drawn. Usually the outlines of the surface and the bottom of the cup are connected by three or four lines. This last detail is unessential, but to my eye they serve to link up the two cup outlines together. Finally a note is made of the depth of the cup in dioptries. In the case of cups where the cup is larger at the base than on the surface, a bracket is made outside the disc margin at the place where this is so, and "bulbous" written there.

To estimate the size of the cup a transparent grid is used. The apparent size of the disc and of the cup surface are found, and the size of the cup expressed as a percentage of the disc.

The question of error in the estimate arises. No opportunity has occurred to compare my results with those of another observer on the same cases. It is estimated that there should not be more than five per cent. error in drawing the disc outlines, and two per cent. in measuring with the grid. This is sufficiently close for clinical purposes.

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\* Received for publication, November 8, 1947.



At the outset it must be pointed out that there are great variations from the average in the sizes, both at the first record and the subsequent occasions, in all age groups. This will be seen in the tables, where they vary from 5 to 100 per cent. And the possible variations are large. If the case of an initial cup varying from 5 to 50, and the final from 51 to 100 be considered the possible variations would be 2,250, which represents the maximum. And the number of eyes—234—multiplied into this will give an idea of the possibilities. Nevertheless, as happens in large collections, the actual cups cluster around the average.

*Fifteen year group.*—This consists of 234 eyes, observed for fifteen years or more, except for five, one of which was observed for fourteen years, and four between fourteen and fifteen years. For these extrapolation was employed, at the last observed rate of growth; it being thought that for so few cases and for so short a time, the total figures would not be vitiated.

TABLE I  
Fifteen Year Groups

Age Groups	Number of Eyes	Average Initial Cups %	Initial Maxima	Initial Minima	Cups at 10 yrs.	Slope of Cups at		Total Slope at 15 yrs.
						10 yrs	15 yrs.	
-10 yrs.	16	23	42	5	39	1.6	45	1.4
11-20 „	22	22	61	7	44	2.2	48	1.7
21-30 „	30	24	53	8	41	1.6	52	1.9
31-40 „	62	26	48	5	43	1.7	53	1.8
41-50 „	60	23	59	7	49	2.6	59	2.3
51-60 „	30	28	57	8	52	2.2	66	2.5
61-70 „	14	28	50	13	45	1.7	60	2.1
Average Slope 1.9								1.9

Table I gives a summary of these eyes. The group cluster around early middle age, for about this time that the social circumstances tend to be more stabilised, and patients are more likely to persist in coming to the same oculist.

As will be seen later, the averages for the early years are rather

high, those for the later too low. The irregularity in the maximum initial cups should be noted; that for the 11-20 years is 61, the highest in the fifteen year group.

The slope is the percentage growth per year of the cups. It is an important measurement, for by this the rate of increase of the cups is ascertained, and the various cups compared with each other. Thus, the ten year group, derived from the fifteen year group by subtracting the growth of the last five years, is found by the slope to have the same value, 1.9, as the fifteen year group. This means that the average increase for the whole term is unaltered; although the individual cups differ from each other.

TABLE II

Alteration of slope (percentage increase of cups per year). Ten year group extracted from the fifteen year group.

Figures in brackets are the number of eyes in the various sub-groups.

Cup size sub-groups	Year Groups						
	-10	11-20	21-30	31-40	41-50	51-60	61-70
1-10 p.c.	2.9 (2)	3.2 (2)	2.9 (5)	2.5 (9)	3.8 (7)	4.6 (1)	—
11-20 „	1.5 (4)	2.9 (12)	2.6 (11)	2.5 (15)	2.5 (19)	2.4 (7)	2.5 (7)
21-30 „	1.7 (6)	1.4 (4)	1.0 (3)	1.5 (26)	2.1 (24)	2.3 (7)	0.0 (1)
31-40 „	0.7 (3)	1.5 (1)	0.9 (4)	1.5 (10)	1.9 (6)	2.1 (13)	0.6 (3)
41-50 „	1.7 (1)	0.2 (2)	1.3 (6)	0.6 (7)	0.6 (1)	1.1 (2)	1.4 (4)
51-60 „	—	—	0.6 (1)	—	0.0 (1)	—	—
61-70 „	—	0.3 (1)	—	—	—	—	—

An interesting condition is seen if the various age classes are separated out according to their cup sizes. In Table II this has been summarised in the slopes for the various values. With seven exceptions, the slopes have arranged themselves in such an order that the smaller initial cups have the higher slopes, the total number of the items being 37. Although some of the subgroups are quite small, the proportion of 30 to 7 is significant, all the more that the discrepancies, 0.2, 1.0, 0.1, 0.1, 0.4, 2.5 and 0.8, have among them three groups which each have only one eye.

This means that the smaller cups tend to catch up the larger, but they are only partially successful. The consistency of these cup

groups is surprising and was unexpected. The smallness of some of the groups, a statistical disadvantage, is counterbalanced by the occurrence of this inverse order in all the seven age groups.

TABLE III

Single Observations—Ten Year Groups—40 eyes in each group.

Year Groups	Average	Maxima	Minima	Slope
11-20	17	49	6	—
21-30	23	39	6	0.5
31-40	26	65	9	0.3
41-50	25	55	11	0.1
51-60	31	75	17	0.6
61-70	35	73	11	0.4
71-80	45	95	9	1.0

*Single observations.*—These consisted of 280 cups, in age groups of 40 each, seven groups in all, beginning at 11-20 years. They are displayed in Table III. The averages for the groups show a steady rise from the first to the last. The maxima are not so regular but show a fairly consistent order; the minima are more irregular they show that in some patients the cups remain small to the end. The slope cannot be stated, as only single observations were made on each case. If the order of the successive groups be taken as the increase per ten years, it will be seen that this agrees fairly well with the average found for the combined group. This single observation group is a better sample than the fifteen year group, for the number in each age group is the same for all ages; in the fifteen year eyes the smallness of the numbers in the early and the late groups decreases their usefulness statistically, unavoidable as this is.

*Combined Group.* With the object of smoothing out the irregularities in the two groups, both were combined together. The ten year groups, from the fifteen year groups, were taken instead of the latter, to conform more easily with the single observation group, which is arranged in ten year groups. From this mixture an average was found, which is used for the final deduction of the average course of

the disc growth. All the disc percentages thus obtained, their age groups being known, may be used, if they are kept in their proper age groups. The ten year cups will have to be included in the next batch to that from which they started. For instance, those derived from the 11-20 year group will have to be included in the 21-30 group for the purposes of this final estimate. Table IV shows the various averages as obtained from the separate groups, and the last set the average as obtained from their combination. (See Chart A).

TABLE IV

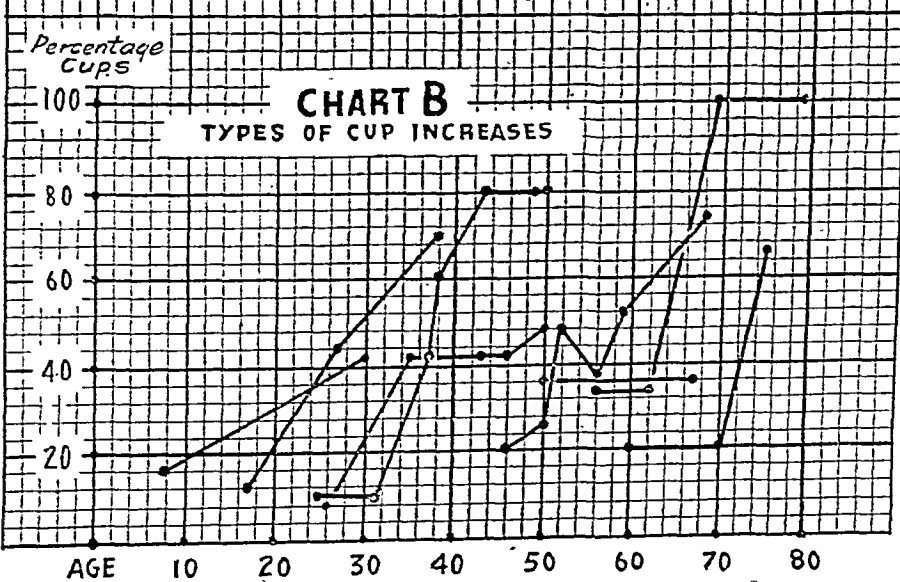
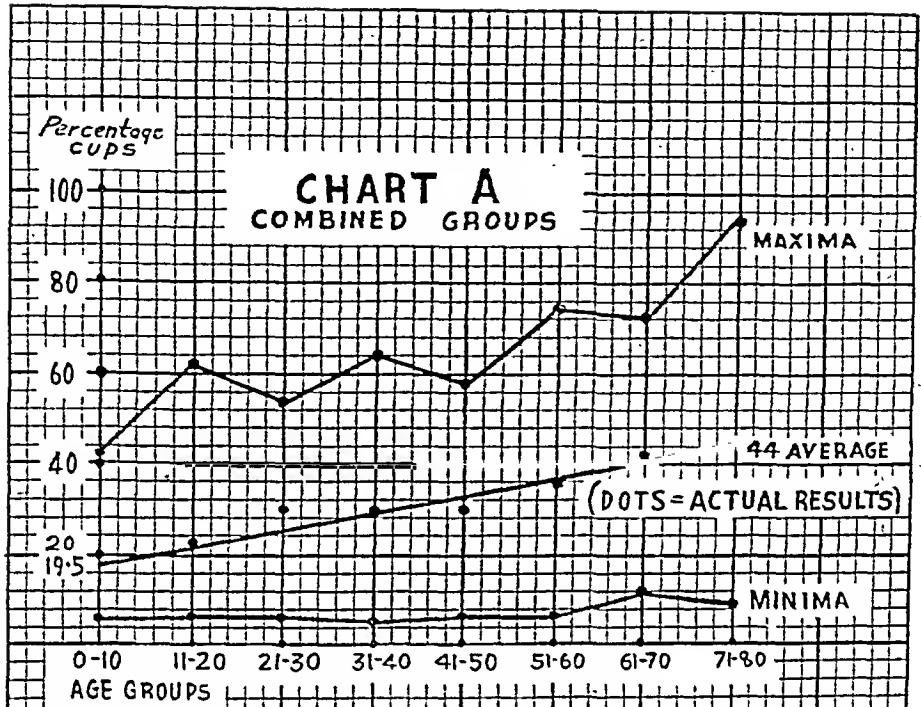
Average cups. Initial, ten year and single observations.

	No of eyes	-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Single observations...	280	—	18	23	26	25	31	35	45
Fifteen year group									
Initial cups ...	234	23	22	24	26	23	28	28	—
Ten year cups ...	234	—	39	44	41	43	49	52	45
Combined average (Initial, 10 yr., and single observations)	—	—	23	29	29	31	36	41	45

*Average slope.* The chart A exhibits the final combined average for the various age groups, they are shown as black dots. They are nearly in a straight line. If a straight line is drawn from 23 (11-20 yrs.) at a slope of 0.35, it will cut the 71-80 yr. line at 44, and, if this is prolonged to the left, as far as the 0-10 column, it will cut it at 19.5. This is an average slope for the disc growth. The general formula is thus:—  $19.5 + (0.35 \times \text{age in years}) = \text{Average cup for that particular year.}$

This formula must be taken for what it states, it is the average between the wide extremes of the maxima and the minima, as shown on Chart A. Nevertheless the nearly straight line shown by the actual figures shows that it is reliable as an average. The figures for the individual cases tend to group themselves around the averages, as should be the case if the latter are representative.

The practical point that follows is that any cup above 70 per cent. should be regarded as suspect, and be considered with the fields and tension before it can be said to be normal. It has seemed to me that a large cup cannot be accepted as physiological unless these precautions are taken.



Decrease in the cups. In one eye the cup was 10 per cent. smaller at the end of fifteen years. Twelve others showed a decrease at some time, though all these were larger at the end of the fifteen years than at the beginning. These temporary losses were 3, 3, 4, 5, 5, 6, 6, 6, 7, 10, 10, and 10 per cent.

One cup was stationary for the whole period, it was 36 per cent. Five others showed very small increases 3, 3, 4, 5, and 6 per cent.

It is not uncommon to have a period of arrest of growth of the cup. This may occur at any period, when first seen, during the increase, or towards the end; examples are given in Chart B, which gives types of cup changes. It will be seen that in some of these the record extends over more than fifteen years.

*Depth of the cups.* Increase in depth tends to happen with the enlargement of the cup area, but irregularly so. It may be stated as a generalisation that if a cup-enlarges to 60 per cent., its depth will increase generally by 0.5 to 1.0 dioptres, but by no means invariably so. A disc may increase to 100 per cent. and yet retain a depth of 1.0 D. An increase to 3 D, with an enlargement of the cup percentage must be investigated by the field and tension.

It is not easy to find any one cause for the cup enlargement. In the early years it can be attributed to the natural growth of the body, but this cannot be the reason for the continuous enlargement which goes on after youth, after the body has stopped growing. It may be other influences come into play which cause the enlargement to continue, which cannot be considered as pathological. Our bodies are always undergoing change, which in ordinary terms would not be thought abnormal, and are considered as part of the processes which lead to old age, yet are not, in general terms, thought to be pathological, though in an exact sense, they are. Perhaps the cup enlargement should be so considered. But this is merely to place it in a group of effects which we do not understand, though well recognised as the approach of old age. In the case of the eye, however, these changes do not affect the attributes of sight, according to the standards applied in the routine of ordinary practice, nor vision as used in every day life. It must be acknowledged that this is an analogy rather than an explanation.

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## A PORTRAIT OF RICHARD BANISTER\*

BY

ARNOLD SORSBY and W. J. BISHOP

LONDON

RICHARD BANISTER deserves well from English ophthalmology. As the editor of the second edition of the English translation of Jacques Guillemeau's *Des Maladies de l'Oeil qui sont en Nombre de Cent Treize aux quelles il est Subject*, and the author of the *Breviary* attached to this edition, he is the first English Ophthalmographer of note. The *Breviary* is a valuable document on the practice of the early ophthalmologist in this country, and is of outstanding historical importance because of an almost incidental passage which gives the first account of hardness of the eye as a diagnostic and prognostic sign. An unpublished manuscript by Richard Banister in the Sloane Collection at the British Museum, discovered by R. R. James, constitutes a further claim on posterity, for it is rich in detail on the social aspect of early English ophthalmology. These aspects of Banister's activities have been recorded fully elsewhere (Sorsby, 1932 (a) and (b); James, 1933; Sorsby, 1933; James and Sorsby, 1934).

James has established that Richard Banister died in 1626. The place and date of his birth are, however, still unknown. As he was admitted to the Company of Barber Surgeons in 1602 and the *Breviary* is dated 1621, when he writes of himself that "it is not long to the period of my daies," he may be assumed that he was at least between 40 and 50 in 1621. This would put his date of birth somewhere at around 1570-80.

A portrait at the Royal College of Surgeons is of interest in that it gives us a likeness of Richard Banister and a definite date of birth—if the authenticity of this picture can be established.

### The portrait

*History.* The Minutes of the Royal College of Surgeons contain the following entry dated June 10, 1841.

Mr. Stanley communicated at the request of Mr. Samuel Barton, of Manchester, a Member, that he Mr. Barton is in possession of an original Painting by Cornelius Jansen, in 1620, of Richard Banister, Author of Banister's *Breviary*; and that if it would be appreciated he would send it to be placed in the Library or Museum of the College.

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\* Received for Publication, April 17, 1948.



FIG. 1.

Photograph of a portrait of Richard Banister, Royal College of Surgeons.





FIG. 2.

John Banister delivering the Visceral Lecture at the Barber-Surgeons' Hall in 1581. (From a contemporary painting now in the Hunterian Library, Glasgow. D'Arcy Power, 1913).

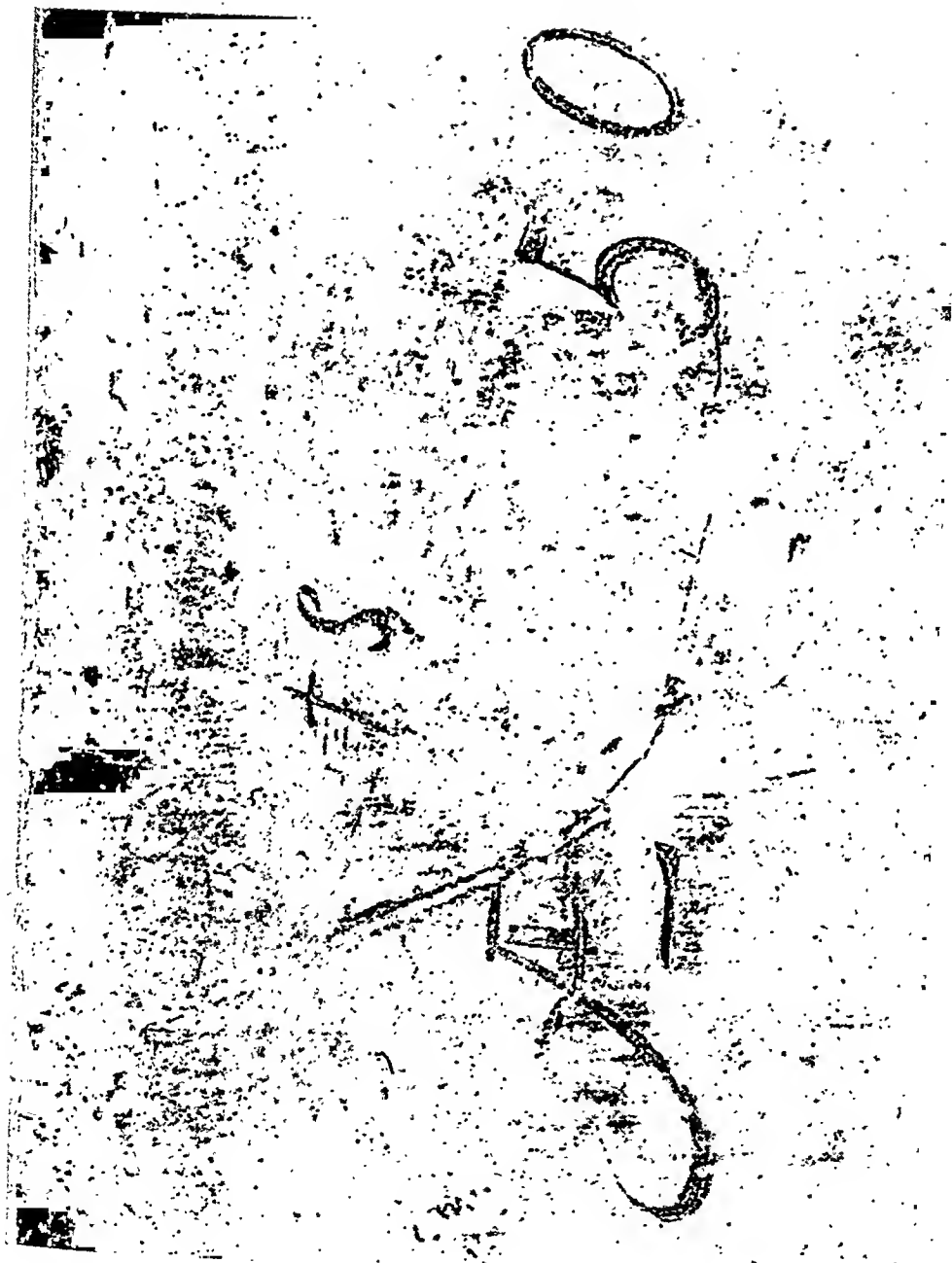


FIG. 3.

Photograph of the inscription in the top left-hand corner of the portrait of Richard Banister.



Resolved :

That Mr. Barton be informed that this Council are obliged by his liberal offer and will be much gratified by the possession of so interesting a Picture.

A month later, on July 8, the following Minute appears :

The Secretary laid before the Council for Mr. Barton of Manchester, the Portrait of Richard Banister mentioned to the Council by Mr. Stanley, at its last meeting.

Resolved :

That the best thanks of the Council be returned to Mr. Barton for such valuable Picture.

The portrait (Fig. 1) has a panel of 35 x 27 in. It has remained in the possession of the Royal College of Surgeons since 1841. In 1866 it was exhibited at the National Portrait Exhibition, when it was shown as a portrait of John Banister "a relative of Richard Banister," and ascribed to Cornelius Jansen. In Hallett's Catalogue of Portraits at the Royal College of Surgeons the portrait is given as that of Richard Banister painted by Van Ceulen; Banister's date of birth is given as 1585 and that of his death as 1633.

These dates and the ascription of the work to Van Ceulen are also given on the frame of the portrait hung in the hall of the College.

*The Conflicting Data.* It has been impossible to trace the history of the picture prior to its acceptance by the College in 1841. From the recorded data the picture might be either of Richard Banister or John Banister; and it would appear that its execution by Cornelius Johnson has not been questioned, for the different names mentioned all refer to the same significant contemporary of Van Dyck. None the less there is no reference to this picture in Finberg's extensive monograph on Cornelius Johnson. The available data therefore give no clear evidence as to the identity of the sitter or of the painter. There is in fact no evidence that it represents either Richard or John Banister.

The suggestion that the portrait represents John Banister can be clearly dismissed. There is a contemporary painting of John Banister in the Hunterian Library, Glasgow (Fig. 2) and this shows no facial (though possibly some family) resemblance to the sitter in this portrait. Moreover the picture carries the date of 1620 and gives the age of the sitter as fifty. Accepting these inscriptions on their face value John Banister must be ruled out for he was born in 1533 and died in 1610.

The possibility that the portrait does indeed represent Richard

Banister is not strengthened by what is known of his life. He was an itinerant oculist, and the highest civic distinction which he is known to have held was that of Churchwarden of Stamford. In his lifetime he was overshadowed by his famous uncle, and subsequently he became one of the forgotten figures of ophthalmology, though the fact that in 1841 Samuel Barton could regard the picture as of medical interest, and the Council of the College "were gratified by the possession of so interesting a Picture" suggests that his reputation was rather higher than present day memory would suggest. Still it remains an open question whether Richard Banister was of sufficient contemporary importance to have had a portrait executed—and that by an eminent painter.

*Internal evidence from the portrait.* These doubts are resolved by a study of the portrait itself, which brings out several things of importance:

(1) The inscription *Ans 50* in the top left-hand corner (Fig. 3) and of *1620* in the right-hand corner.

(2) The cross to the right of the inscription *1620*.

(3) The box held in the sitter's left hand.

(4) The box at the side of his left hand.

(5) The instrument held in his right hand.

As for the two dates, authorities accept dates on portraits on their face value unless there is reason to doubt them. The fact that the shape of the ruff is that in fashion c. 1618-1632 (as Mr. C. K. Adams informs us) would justify accepting the validity of these inscriptions. Strong evidence that the sitter was a Banister comes from the cross in the right-hand corner. An illustration of this particular cross is given in Guillim's *A Display of Heraldry* (1638) under the designation of a cross flory. Edmonson's *A Complete Body of Heraldry* (1780) shows the arms of several branches of the Banister family; the arms of the Banisters of Leicester are given as a cross patonce, whilst those of another Banister without locality has the arms of a cross flory. The identification of the sitter as a Banister is further strengthened by the initials R.B. on the box at the side of the left hand, whilst the box held in that hand shows the first initial clearly, the second being covered by the hand. The possibility of the sitter being Richard Banister therefore becomes more tangible. If it could be proved that the instrument he holds in his right hand is a couching needle the evidence for the picture representing Richard Banister becomes fairly conclusive.

If the evidence for the identity of the sitter supports the traditional information on the picture, no such support can be obtained for the authenticity of the portrait as the work of Cornelius Johnson. On this technical issue we are obliged to Mr. C. K. Adams

for the following note, which he kindly prepared after studying the picture when it was removed from the frame and photographed.

"The portrait is a contemporary work having affinity to the work of native-born artists. It has been attributed to Cornelius Johnson. It is not, however, by such a skilled painter nor is the brushwork and colouring akin to his. It has suffered comparatively little at the hands of restorers and appears to be in all essentials, apart from the inscription, as originally painted.

- The costume and type of ruff depicted are of between 1618 and 1632 and one might guess the sitter's age as being 45 or so. There is therefore no reason to question the date and age as inscribed on the portrait on these scores, though they have been very largely repainted. This is very apparent in the case of the A in "A<sup>ts</sup>" where there are now visible three cross strokes to the A and two down strokes on the left hand side. "Originally there was apparently a diphthong 'Æ' on a smaller scale than the more modern 'A.' The 'ts' is of the same date as this alteration. There is room for the whole word 'Ætatis' before '50' if written on the scale of the original 'Æ.' Part at least of the date 1620 is not the original paint as an old crack running down through the figure '2' has had to be made good on the surface to a width of half an inch. The '2' and half the '0' are certainly not original. Above the inscription 'A<sup>ts</sup> 50' and about half an inch away from the top edge there is a mark which is highly suggestive of an inscription which has been almost entirely scraped away. Insufficient is left to read even a single letter. The appurtenances such as the instrument which the sitter holds, and the instrument boxes, and also the initials on the boxes appear to be contemporary with the original painting."

It may therefore be accepted that the portrait does indeed represent Richard Banister and it follows that the date of birth can be placed at 1570. This fits in with the indirect evidence previously available. To the appreciation that the Council of the Royal College of Surgeons expressed to Samuel Barton in 1841 for presenting the picture to the College, posterity may now add its own thanks for preserving this picture as a national treasure. Samuel Barton had a double interest in the portrait. He himself was one of the early surgeons to the Manchester [Royal] Eye Hospital, to which he was appointed in 1815. He died in 1871 after achieving local distinction as an ophthalmic surgeon, and as an enthusiastic collector of pictures and engravings.

We are indebted to the President and the Council of the Royal College of Surgeons for permission to study this portrait and for publishing this note; to the Secretary of the College for kindly

tracing the relevant Minutes, and Mr. S. Wood of the Library staff for information on Cornelius Johnson. To Mr. C. K. Adams, Assistant to the Director of the National Portrait Gallery, we are greatly obliged for the trouble he has taken, and for his ready guidance. We are also indebted to Mr. F. N. L. Poynter and Mr. C. A. Earnshaw of the Wellcome Historical Medical Museum for their interest and help. To Dr. O. M. Duthie and Dr. E. Bosdin Leech of Manchester we are obliged for their help in the fruitless search for the history of the portrait prior to its presentation to the Royal College of Surgeons.

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## SOME NEW POINTS IN THE TECHNIQUE OF IMPLANT IN TENON'S CAPSULE AFTER ENUCLEATION

BY

ALBERT FAVORY

PARIS

IN some cases the implant of "acrylic" or any other material within the sclera after evisceration is not advisable, especially when sympathetic ophthalmia is threatening; enucleation is then absolutely necessary, and an implant in Tenon's capsule with fixation of the four recti can be done to obtain a moving prosthesis.

An implant within the sclera gives better movements to the prosthesis owing to the fact that the six ocular muscles are keeping their mobility even admitting that they are weakened more or less after the operation.

Among the numerous techniques described, Cutler's operation presented at the recent Oxford Congress appears as very seductive and exhibits very good functional results. Nevertheless, our personal

technique differs from Cutler's operation in many ways. The size and shape of the implant as well as the material used are not quite similar, so we shall emphasize these points of importance.

The fact that we should foresee a certain amount of shrinkage of Tenon's capsule after the operation led us to the opinion that the implant ought not to be too large; a ball of 10 mm. diameter is

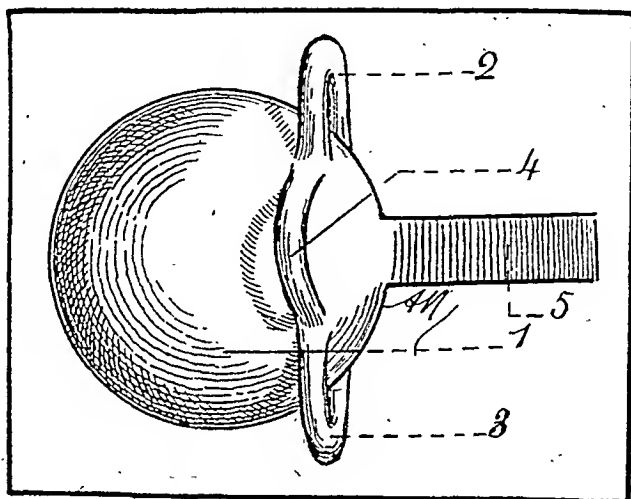


FIG. 1.

(After Virenque). Side view of implant. 1, body. 2, 3, 4, arches. 5, spur.

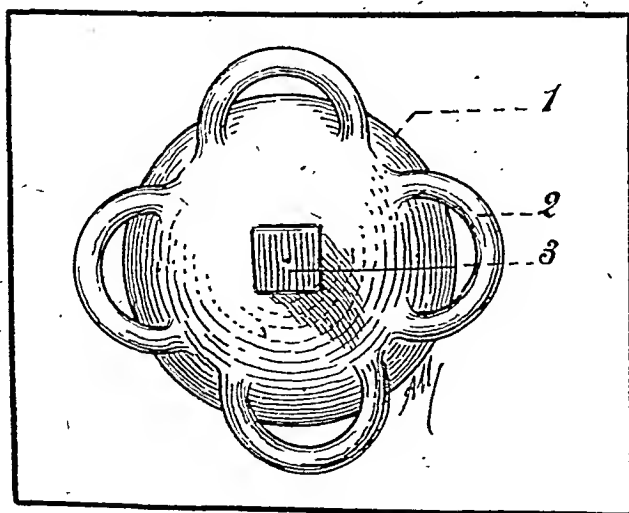


FIG. 2.

(After Virenque). Face view of implant. 1, body. 2, arch. 3, spur.



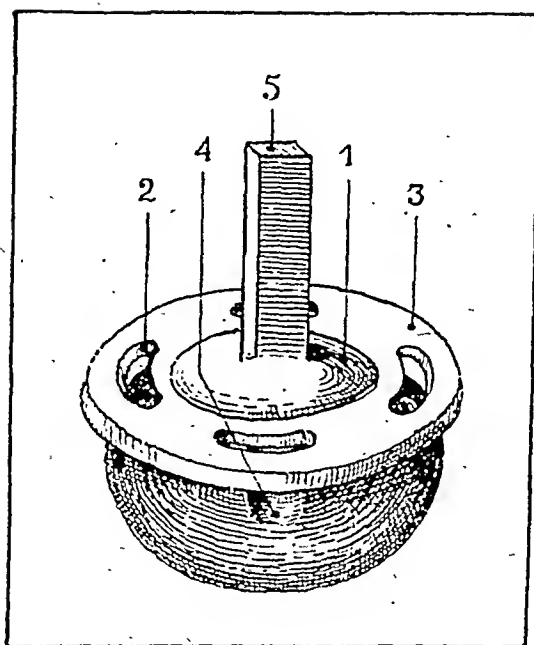


FIG. 3.

Face view of implant (new shape). 1, body. 2, oval-shaped hole. 3, disc. 4, groove. 5, spur.

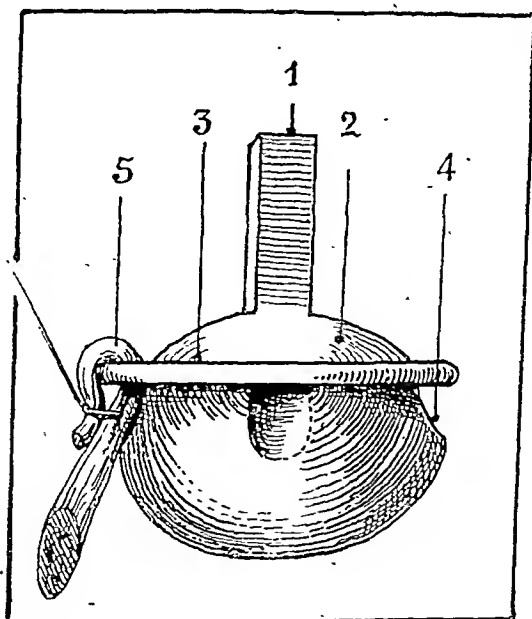


FIG. 4.

Side view of implant (new shape). 1, spur. 2, body. 3, disc. 4, groove. 5, muscle loop.

sufficient, an excessive diameter may be the cause of its subsequent extrusion.

The only material used in our technique is "acrylic"; we think that the addition of a golden ring and pin makes the piece too heavy, and probably gold is not as well tolerated as acrylic, notwithstanding the fact that gold is a very rare material here in France.

Our implant is spherical in shape, its posterior surface being slightly flattened; four little arches of the same material as the ball are fixed near the anterior surface to receive the tendons of the recti. On the anterior aspect a spur of 15 mm. long and quadrangularly prismatic in shape is protruding (see Figs. 1 and 2). In a new shape the muscles are fixed on a disc with oval-shaped holes. On the implant body are four grooves to ease the muscle looping (Figs. 3 and 4). The operation is done with local anaesthesia, using a 2 per

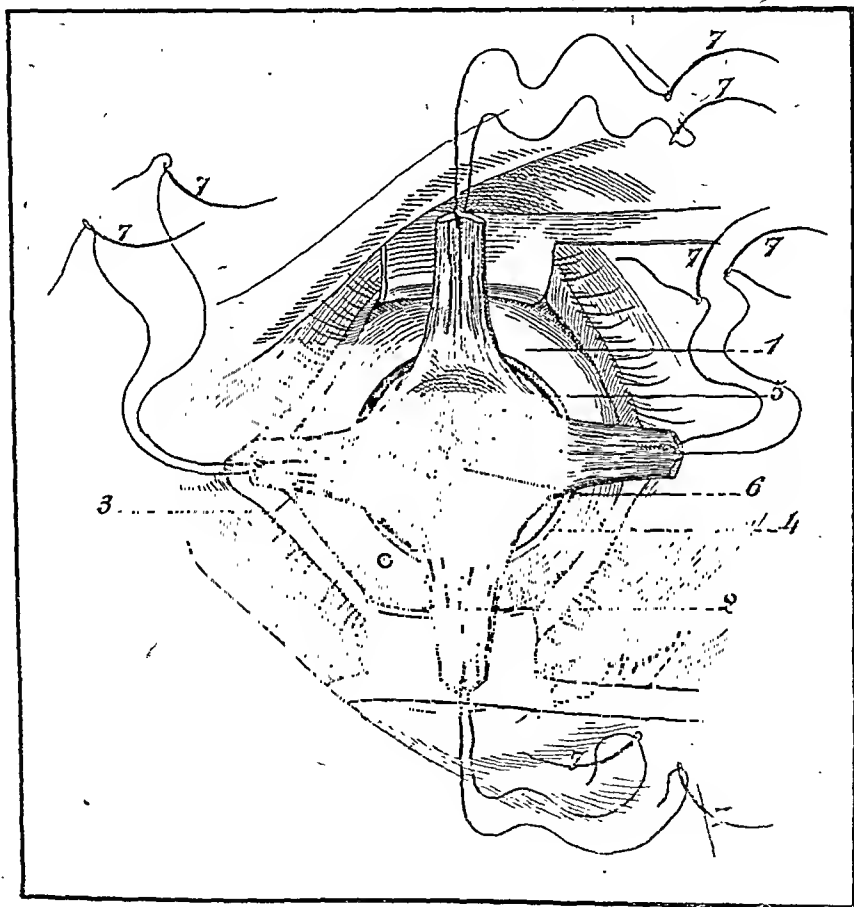


FIG. 5.

Enucleation complete (after Virenque) 1, 4 and 5, orbital tissue. 2 and 3, rectus muscle. 6, Tenon's capsule. 7, double armed silk stitch.

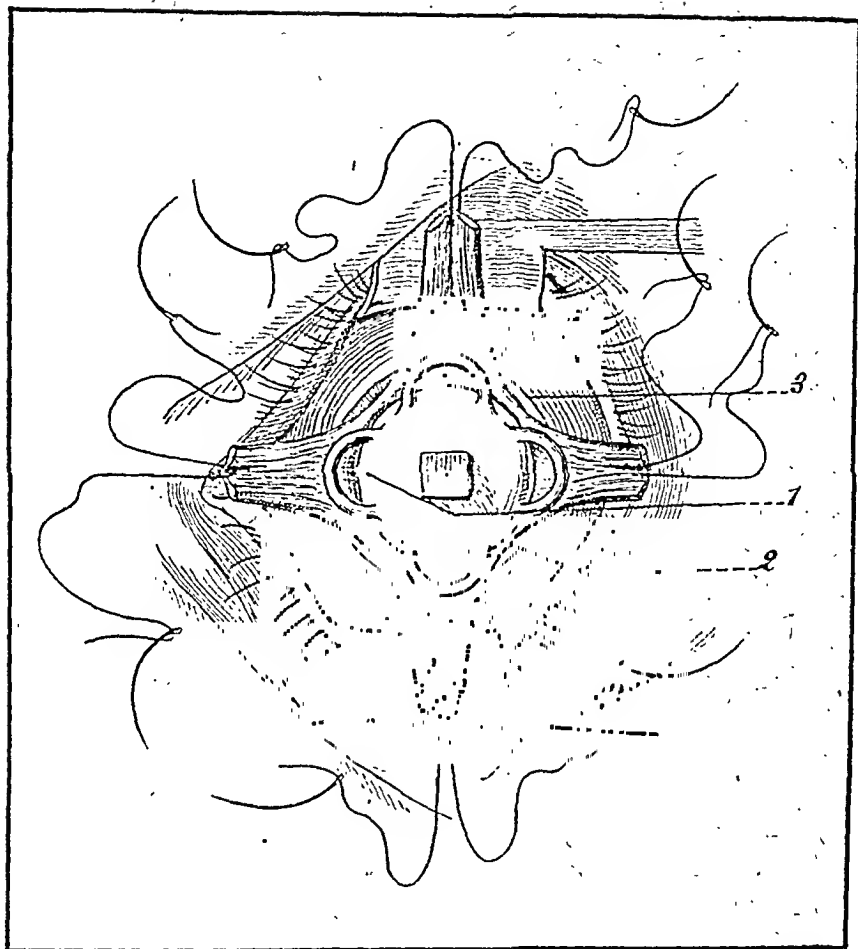


FIG. 6.

Implant placed in Tenon's space (after Virenque). 1, implant. 2, Tenon's capsule. 3, orbital tissue.

cent. solution of novocaine adrenalin for a retro-bulbar injection. It is not necessary to add to this solution 1 c.c. of 40 per cent. alcohol as is done in evisceration. The local anaesthesia is completed by injecting a few drops of the same solution within each rectus and subconjunctivally around the limbus. To keep the patient absolutely quiet, a subcutaneous injection is done one hour before the operation with nargenol (a mixture of morphia, scopolamine and ephedrine). We never use general anaesthesia.

The enucleation is performed in the usual manner, but a double armed silk suture is passed through the tendon of each rectus after this has been hooked. Then the eye is delivered, Tenon's capsule is inspected and haemostasis is carefully done with R.C. haemostatic (the main basis of this solution is extracted from pigeon muscle) (Fig. 5).

The implant is held in place in Tenon's capsule by grasping the spur with the forceps (Fig. 6).

The suture holding each rectus tendon is passed through each corresponding arch or hole, the tendon is then looped through round the arch or disc, the two needles of each suture being passed through the tendon and the silk passed through the conjunctiva and tied over (Fig. 7).

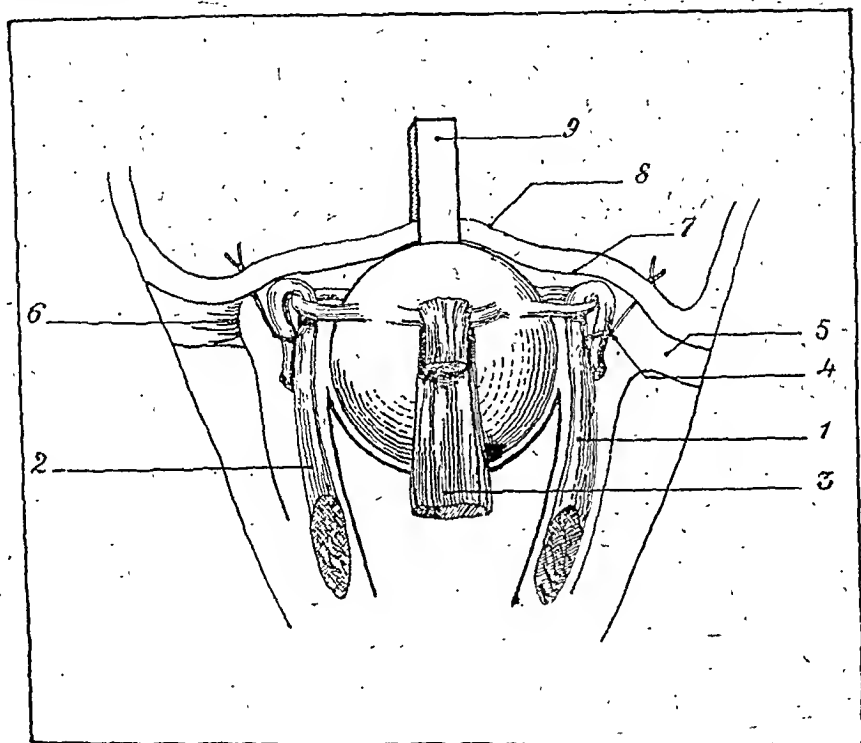


FIG. 7.

Semi-schematic cut of socket. 1, 2, 3, rectus muscle. 4, muscle stitch tied over conjunctiva. 5, Tenon's space. 6, socket space. 7 and 8, conjunctiva. 9, spur.

Tenon's capsule is sutured by separate catgut stitches and must be very carefully closed, conjunctiva is sutured over by five silk stitches each side of the spur (Fig. 8).

It seems that suturing the conjunctiva over the implant does not alter the deepness of the fornices owing to the conjunctiva's great elasticity.

At the end of the operation only the spur is protruding out of the conjunctiva and will later on enter a hole on the posterior surface of the prosthesis. A retainer shell is placed inside the lids to hold the implant and maintain the depths of the fornices.

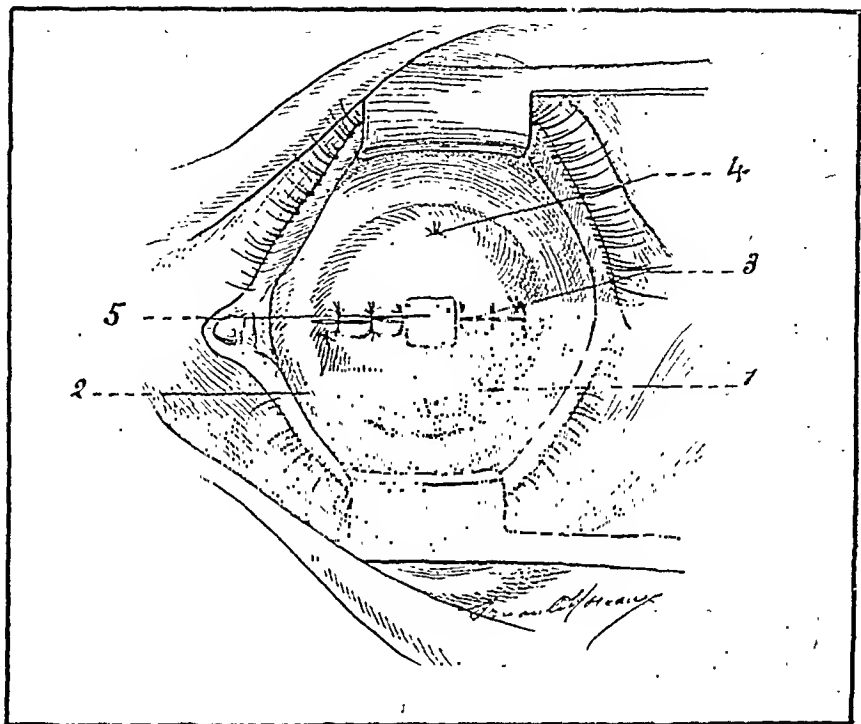


FIG. 8.

Completed operation (after Vireneque). 1, implant covered by conjunctiva. 2, conjunctiva. 3, conjunctival suture. 4, rectus suture. 5, spur.

Very little reaction follows the operation and the dressing is not changed until after six days. The stitches are removed after ten days and a mould of the anterior aspect is done. The posterior surface of the prosthesis is made from the mould and will then fit perfectly well.

The shell is removed and the prosthesis is inserted as soon as possible, even if it is a provisional one to maintain the shape of the fornices. The final prosthesis may be adapted some weeks later. It is too soon to judge of the final value of this technique, as we have performed only a few operations.

We observed elimination of the implant in our first case. This was a bad case with an abnormal socket, and the piece used was too large. In another case the implant became prolapsed owing to the lack of firm suturing of the muscles. We had used catgut instead of silk to fix the muscles. In the other cases we were satisfied with the functional and cosmetic results.

We look forward to proceeding in this way and improving our technique by making any necessary modifications to ease its performance and to better its results.

## ANNOTATIONS

## The Passing of the Gratis Patient

When the writer started his practice the chink of the golden sovereign and silver shilling could still be heard in the land. Later, the rustle of the Treasury note superseded this comforting sound. In future it looks as if the only rustle to be heard in our consulting rooms will be that of the various certificates we shall have to complete. It is a solemn thought that after July 5, 1948, the gratis patient will have passed away. Some will perhaps say, with Mrs. Gamp, that it will make a lovely corpse; but our personal feeling will be one of regret.

Up to now a proportion of our work has always been on the free list; members of our own profession, their wives and families, the nursing sisterhood, curates and many of the poorer clergy, with those of small means whom we were asked to see by friends or patients. Provided we did not get too many gratis patients in any week we did not complain. You never knew what might turn up and even if it were nothing more exciting than a patch of opaque nerve fibres your time was not wasted.

A gratis patient and a grateful patient are not always synonymous terms, but very often they are, and among the writer's pleasant recollections are those of unsolicited thanks received from such people. Those of us who worked at Moorfields on Mondays and Thursdays in the early years of this century will recall how Sir Arnold Lawson's desk was usually piled high with bunches of flowers, a tribute alike to his professional ability and kindness of heart. We fear that in future these floral tributes will largely disappear along with much of the competition and friendly rivalry of the past. Emergencies in the streets will, we suppose, still be handled by the police and ambulance service. It would be highly improper were an apoplectic fit to be left in the gutter like a dead cat until his own medical attendant could be found.

The retired doctor is usually on the free list of some colleague. For the minor ills of life he can treat himself. Can he in future order himself ten grains of aspirin or will he have to attend a clinic and get a prescription? Should the writer get a mild conjunctivitis might he treat himself, or must he be "zoned," like fish, to the nearest ophthalmic surgeon? When that celebrated lawyer, Sir Edward Coke, was sent to the Tower by James the First he was told he might have legal assistance for his defence if he wished. His reply was—"I know myself to be accounted to have as much skill in the law as any man in England and therefore need no such help"; and, in the matter of a mild conjunctivitis, we must say we feel much the same. Perhaps, after all, as the undergraduate is

reputed to have written at the end of a Latin prose essay\* : *hae autem observationes neque hic sunt neque illic*. But these remarks are neither here nor there. We merely throw them out for consideration, in placing this wreath upon the tomb of the gratis patient.

\* Herbert Paul.—"Men and Letters."

### Emotional Responses

It is an old saying that laughter and tears are near akin to each other. On the whole we think that in most people the risible element is more easily stimulated than the tearful, and perhaps also the more easily controlled. Pathetic passages in prose or verse may lead to weeping in some cases; parodies of the same will certainly lead to laughter and to tears only if one laughs too much.

Those who remember "Tom Brown's Schooldays" will recall George Arthur bursting into tears while construing a passage in the Iliad and the comments of his schoolfellows afterwards at his exhibition. In his case the stimulus would seem to have been partly visual and partly aural. Schoolboys as a rule are more likely to be risible than tearful; but we can remember an occasion in our own schooldays when the form was stumbling through the "Retreat from Syracuse" and making a hash of it. Suddenly the form master started to read us the Greek. The form was very nearly reduced to tears as a result. Speaking for oneself, one seemed to hear the wailing of lost souls as he was reading the passage. In this case the stimulus must have been an aural one, for most of us could have stared at the text all day without getting either the sense or any emotional response at all.

Belloc's Lord Lundy had the tearful response so well developed that he could not answer the simplest question without weeping. Ophthalmology at first sight does not seem to offer much scope for either response. But we must confess that there was an occasion on which we experienced a queer lacrymatory feeling long ago, when we were working through Fuchs' Lehrbuch, in order to try and teach ourselves to read German ophthalmology. It was in the account of the end results of amyloid degeneration of the conjunctiva. The English was a plain matter of fact statement: "Then is the eye lost." But the juxtaposition of "Augen" and "verloren" seemed more sonorous than the English equivalent and we suppose accounted for it.

A Scottish friend of ours once said that he could never read "Rab and his Friends" without tears. Many will agree with this instance.

The works of George Eliot abound in instances where the risible response is stimulated and in the "Scenes of Clerical Life" will be found examples where the tearful may come into play.

We do not think that our own pages ever stimulate a tearful response but there may be occasions where words have been misspelt or punctuation marks omitted when we provide the careful reader with a source for laughter.

In reading to oneself the brain not only sees the words, but must receive a kind of subconscious apprehension of what the passage will sound like if articulated in order to get the sense of the sentence. Visual, aural and mental processes must partake in some way to raise an emotional response of either kind. We confess that these waters are too deep for us to sail on, but some idea of what we intend is found in one of Charles Lamb's letters to Bernard Barton, the Quaker poet. "I can hardly read a book, for I miss the small soft voice which the idea of articulated words raises (almost imperceptibly to you) in a silent reader. I seem too deaf to see what I read. But with a touch or two of returning zephyr my head will melt."

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## OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

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THE 68th Annual Congress of the Ophthalmological Society of the United Kingdom was held on April 8, 9 and 10, at the Royal Society of Medicine, London. Over 200 members and many distinguished continental visitors, including the following, were present:—Professor Marc Amsler, Professor J. W. Nordenson, Professor H. Ehlers, Professor J. van der Hoeve, Dr. E. Pflueger, Professor E. Velter, Professor H. J. M. Weve, Professor A. Franceschetti, Professor Applemans, Professor W. H. Melanowski, Dr. H. Sjogren, Dr. T. L. Thomassen, Dr. A. C. Copper.

After a short opening speech by the President, Dr. A. J. Ballantyne, the topic for the morning's discussion, "Subjective Disorders of Vision (excluding those due to local ocular disease)," was introduced by Professor H. Cohen in a communication that was interesting, well-balanced, and beautifully delivered, followed by Dr. Denis Williams, who contributed also some original and important observations on the nature of "macular sparing" that showed an enviable mastery of the more recondite methods of perimetry; and by Mr. J. H. Doggart who continued ably and agreeably on this interesting subject. The discussion that followed could not maintain the high level of excellence that marked the opening speeches. A number of observations, interesting and sometimes entertaining, were offered.

The Bowman Lecture was delivered this year by Professor Marc Amsler. The subject chosen was "New Clinical Aspects of the Vegetative Eye," a clear and impressive thesis on the clinical and



scientific value of biochemical and biophysical micro-analysis of the aqueous fluid. These were beautifully illustrated by a film. Evidence was also given of the blood aqueous barrier, by the delay in appearance there of systemic fluorescein on slit-lamp microscopy, in chronic glaucoma, uveitis and systemic affections. The bearing of this in assessment of disease was illustrated.

The following papers were read during the Congress and covered a wide field :

"Ocular Palsies due to infection of the Nasal Sinuses" by Helen Dimsdale and D. G. Phillips; emphasising with case histories the frequency of sinusitis as a cause of ophthalmoplegia, either coincidentally by toxic effect, due to direct pressure of chronic sphenoiditis or due to periostitis of the superior orbital fissure.

"A Preliminary Survey of Forty-five Consecutive Cases of Congestive Glaucoma" by J. P. F. Lloyd; concluding, *inter-alia*, that acute glaucoma does not often cause as acute symptoms as those classically described; that those cases with gross visual loss may well have a thrombotic factor; that recurrences are rare although gonioscopy shows obliteration of the angle of the anterior chamber after iridectomy; stressing the inadvisability of using eserine after trephines, and the fundamental difference between acute and chronic glaucoma.

"The Conjunctival Naevus and the Neurogenic Theory of Melanomata" by Eugene Wolff; discountenancing the neurogenic theory of their origin.

"Pictorial Demonstrations of Spasm of the Central Retinal Artery, Entoptic View of Retinal Vascularization, Hypophysial Tumour Causing Homonymous Hemianopia and III Nerve Paralysis, and Depigmentation of Iris in Chronic Glaucoma" by H. M. Traquair. In discussing these, E. Kraupa described how it was possible to see 2 or 3 vascular entoptic shadows, using 2 or 3 lights, and M. W. Paterson showed drawings of entoptic vessels that suggested a vascular raphe to the nasal side of the central avascular area.

"The Venous Pressure in Glaucomatous Eyes" by T. L. Thomassen. By ocular tonometry and manometry of the episcleral veins, venous pressure was shown to anticipate a rise or fall of intra-ocular pressure, the outflow of aqueous in aqueous veins being observed to be hampered as pressures are increasing and *vice versa*.

"Some Observations on Clinical Perimetry" by G. I. Scott.

"Cases of Subconjunctival Rupture of Globe by a Cow's Horn, and Arterio-venous Aneurysm" by G. T. W. Cashell, the former showing remarkable recovery of a disorganised eye with an avulsed iris, and contrasting with a case at the clinical demonstration of total iridectomy effected by a jackdaw. Two cases similar to the latter were demonstrated by A. Franceschetti.

"Papilloedema in Association with Toxic Hydrocephalus" by A. G. Cröss. Follow-up of 32 cases showed only one case of optic atrophy and four of arcuate extension of the blind spot, and confirmed the inadvisability of early decompression.

"Latent Nystagmus" by T. Keith Lyle; six case histories of this condition in association with concomitant squint, emphasising the importance of binocular vision testing, and the undesirability of occlusion in such cases. A film was shown.

"The Classification of the Unassociated Dystrophies of the Fundus" by Professor Arnold Sorsby.

"Pictorial Demonstration of Pressure Grafting in the Contracted Socket with plunger anchored to a dental cap-splint, Epibulbar Dermoid, and Gummatus Ulceration of the Eyelids" by J. Ellison.

"Prognosis in Detachment of the Retina" by C. Dee Shapland, analysis of 155 cases.

"The Mode of Development of the Vascular System of the Retina with Some Observations on its Significance for Certain Retinal Diseases" by I. C. Michaelson. Retinal vessels originate by budding from other vessels, the capillaries from veins not arteries; hence in diabetes the veins and capillaries are principally affected, in hypertension, the arteries.

"Atropine in the Treatment of Glaucomatous Iridocyclitis" by Professor W. H. Melanowski. Six cases were discussed.

"Auto-Eversion of the Upper Lids" by W. C. Souter, film with anatomical discussion, an agreeably light note for the conclusion of the Congress.

A Joint Clinical Meeting was held in association with the Ophthalmological Section of the Royal Society of Medicine at the new Institute of Ophthalmology, and cases of interest were shown by Dr. Mary Cripps, Mr. A. G. Cross, Mr. A. C. L. Houlton, Mr. E. F. King, Mr. T. Keith Lyle, Mr. S. Philips, Mr. H. Ridley and Mr. P. Trevor-Roper.

A Trade Exhibition of ophthalmic instruments was also held during the Congress.

The Annual Dinner of the Society was held at the Royal College of Surgeons by kind invitation of the President and Council of the College. Professor Henry Cohen proposed the toast of the Society with polished urbanity, and the President replied. Mr. C. B. Goulden then welcomed the guests, who included Sir Alfred Webb-Johnson, Air Vice-Marshal P. C. Livingston, Sir Wilson Jameson, Sir Stewart Duke-Elder, Dr. A. F. MacCallan, Mr. F. A. Williamson-Noble, Professor Henry Cohen, Dr. Denis Williams, Mr. Frank W. Law, Mr. A. H. Levy, Mr. D. G. Phillips, Dr. Helen Dimsdale, and the foreign visitors already mentioned. Air Vice-Marshal P. C. Livingston, the Director-General of the R.A.F. Medical Service replied. Dr. H. M. Traquair toasted the President, and Sir Alfred Webb-Johnson closed the evening with an anecdote.

## BOOK NOTICES

**Diseases of the Eye.** By SIR JOHN HERBERT PARSONS and SIR STEWART DUKE-ELDER. Pp. viii and 732. 21 plates. 368 text figures. London, J. and A. Churchill, 1948. Eleventh edition. Price 30/-.

It is in the nature of things that books relating to current medical practice tend to be almost ephemerides, not indeed creatures of a day, but equally not possessed of that diuturnity owned by some of the more philosophical of physicians' works. This must be so, for such books not only contain a foundation of basic and unchanging scientific fact, but must also be cognisant of that mass of new knowledge and theory which scientific research and clinical experience remorselessly accumulate; should they fail in this, they will inevitably be relegated to the dust and silence of the upper shelf to be superseded by the latest and most up-to-date work.

"Diseases of the Eye" is an old friend, not one of those who are never seen with new faces, yet one who, born again and again in the course of its forty-one years of life, retains its own essential character. In this process of palingenesis the book has contrived to keep abreast of developments as they occur with a balanced judgment and eclecticism which contribute no little to its value; new knowledge has not been included until its worth and importance have been proven, and new theories and methods of treatment have not been described simply because they are new.

To say that this edition of the work, under the joint authorship of Sir John Parsons and Sir Stewart Duke-Elder will be as welcome as have been in turn its ten predecessors, will be sufficient recommendation to the many of us who are already familiar with it. For those whose acquaintance with the literature of Ophthalmology is embryonic, one may say that as an introduction for students, general practitioners and junior ophthalmic surgeons, its value can hardly be exaggerated. With considerable economy of words it contains a mass of facts on anatomy, physiology, disease, treatment and the medical aspects of ophthalmology which will be of the greatest use to students and practitioners, and, when digested and illumined by clinical experience will advance the junior ophthalmic surgeon far along the path of his specialty.

The new edition closely follows the layout of its predecessors. More space is devoted, in view of their now proven value, to chemotherapeutic agents, although description of the well tried classical methods of treatment has not been omitted. The chapters on the neurology of vision and diseases of the nervous system have been revised, and diseases newly noted include epidemic keratoconjunctivitis, toxoplasmosis, brucellosis, and exophthalmic ophthalmoplegia;

certain recent advances in operative technique, such as Barkan's operation of Gonio-trabeculotomy are also mentioned. Altogether the book well fulfils its avowed object of being a safe, reliable and at the same time, modern introduction to diseases of the eye.

**Handbook and Atlas of the Slit-Lamp Microscopy of the Living Eye.** By ALFRED VOGT. Second Edition, Vol. III, Iris, Vitreous Body, Conjunctiva. 344 pages. 985 figs. (mostly in colour). 1948., Schweizer Bruck u. Verlagshaus, Zürich (H. K. Lewis, London). Price £16 10s. 0d.

As in all branches of human knowledge, so in medicine, great books are scarce and are to be treasured as fine gold. To this category belongs Alfred Vogt's Handbook and Atlas of the Slit-Lamp Microscopy of the Living Eye. As is now well-known, when Gullstrand first demonstrated the slit-lamp to the German Ophthalmological Society at Heidelberg in 1911, it is no exaggeration to say that a revolution was brought about in clinical ophthalmology. Since Gullstrand's early instrument was introduced a number of technical improvements have been made, not the least of which was the rearrangement of the illumination to provide brilliant and uniform optical sections of the tissues, a technique introduced by Vogt in 1920. Owing to its ease of access and the transparency of many of its tissues, the eye is thus available for examination in minute detail such as is attainable in no other part of the body; a microscopy of the living free from the mutilating technique of the morbid histologist is rendered possible, and the early signs of disease or the finer points of diagnostic or prognostic significance are determined in the eye with a certainty unobtainable in earlier days or in other organs to-day. The unflagging industry, sustained enthusiasm, and the brilliant and critical clinical acumen of Vogt, aided by a team of gifted colleagues in his clinic in Zürich and by unusually talented artistic assistance, made him the ideal exponent of the new method, and for a decade his clinic became the Mecca of ophthalmologists from the world over. From his clinic there poured a continuous stream of papers, many revolutionary in their observations, and these were collected and systematized in his "Atlas," the first edition of which appeared as a single relatively small volume in 1921. But as observation succeeded observation in greater and greater detail and time added significance to their value, a second edition of the book began to appear, the title changed from "Atlas" to "Lehrbuch und Atlas," and the size increased from one to three large volumes. The first, containing 692 illustrations with an abundant explanatory text on clinical methods, the cornea and anterior chamber, appeared in 1930; the second, bringing the number of illustrations up to 1507, is without doubt the most complete and authoritative treatise on the lens ever written; the third, bringing the number of illustrations up

to 2346, dealing with the iris, vitreous body and conjunctiva, is the volume under review. The first two volumes were written in German and published from Berlin: it is a sign of the times that the third is written in English and published from Zürich. The writing was completed in 1941 before Vogt's death, and the appearance of the book has been delayed for seven years.

In the space of a brief review it is impossible to give an adequate appreciation of this work, for it is unique in any branch of medicine. All the classical conditions are minutely described with abundance of case histories lavishly illustrated, and in addition there is a large number of new observations and new associations. Thus in connection with the pupillary border the efflorescences appearing in heterochromic iritis and the cysts arising from the long application of pilocarpine are described for the first time. The morphology of the pathological vitreous body takes on a new and unexpected interest as well as the part this structure may play in the formation of retinal holes in cases of detachment. Of great practical importance is the detail of the differential diagnosis which long-followed-up observations by the slit-lamp have rendered possible between simple and malignant pigmented tumours of the iris. A feature of the book is the stress laid upon genetics and hereditary conditions, one of Vogt's major interests. In this respect he has made a feature of the long-term study of the eyes of twins. His conclusions are of great interest, for example, that the microscopic details of the iris and their behaviour in extreme old age are pre-determined in the germ-plasm. Moreover, in a supplement to the study of the lens included in this volume, based on an imposing amount of evidence of the same nature whereby identical changes shared by monozygous twins are hereditary while variations are due to exogenous influences, he concludes that senile cataract is a phenomenon of ageing determined hereditarily on an exact parallel with greying of the hair or wrinkling of the skin. He follows out the interesting suggestion that the influence of medicaments on the formation of cataract can best be controlled by administering the medicament to one twin, the other being used as a control.

Vogt was a man of very decided views and with some of his theories it is reasonable to disagree; but he was one of the finest observers of this generation and no one can question his factual data. To anyone interested in ophthalmology or genetics this book will be found invaluable and indispensable; to the more general reader it is an object-lesson in scientific observation at its highest level enthusiastically applied and followed up. It is expensive to buy, but a book of this type is expensive to produce and in terms of value the price is cheap.

## CORRESPONDENCE

## BAILLIART'S DYNAMOMETER

*To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.*

DEAR SIRS,—May I congratulate Mr. Foster on his valuable description of the continental clinics, but on one point only I disagree. I have used Bailliar's dynamometer for over fifteen years and I find this a reliable and important method in measuring the arterial tension in different branches of the vascular tree. The method is not easy, but once mastered is as precise as measuring of the blood pressure by a sphygmomanometer. I am usually satisfied with an approximate measurement without taking the intra-ocular pressure as well.

I am, Sir,

Your obedient Servant,

N. PINES.

41, PHILPOT STREET, E.1.

April 16, 1948.

## OBITUARY

## H. SECKER WALKER, F.R.C.S.

*Ophthalmic Surgeon, The General Infirmary at Leeds.*

*April, 1863 — February, 1938.*

BORN in 1863, the second son of Dr. Thomas Walker of Wakefield, Secker Walker was educated at the Grammar School of that city, and at University College Hospital, London.

Shortly after his appointment as Hon. Asst. Surgeon to the Eye, Ear, Nose and Throat Department of the General Infirmary at Leeds in 1890, he spent six months in Vienna, and after returning was one of the first Englishmen to perform a mastoidectomy.

From 1912, on the division of Ophthalmic and Aural Departments at the Infirmary, he confined his practice to ophthalmic surgery.

In 1914, H.H. The Jam Sahib of Nawanager (the immortal Ranji) became his patient, after a serious grouse-shooting accident, and in gratitude for his recovery, in addition to naming a ward after Secker Walker in Nawanager Hospital, "Ranji" provided the Leeds Infirmary with a new ophthalmic theatre, and out patient department. The design of these incorporated many of Secker Walker's own ideas.

A keen Territorial from the founding of the force in 1908, he carried on the eye departments of the East Leeds and Beckett Park Military Hospitals from 1914-1918, being presented to His Late Majesty King George V at each of the Royal visits.

He was instrumental in persuading the authorities during this period to accept large numbers of men who had been rejected for defects that would be considered trifling in soldiers today.

Appointed Consulting Surgeon in 1919, he retired to the south, but kept up his professional activities, as a member of the Committee of the Bath Eye Infirmary, Pensions Secretary of the Wiltshire Association of the Blind, and as moving spirit and Chairman until 1939 of the Foundation Committee of the Bradford-on-Avon District Hospital.

His last public appearance was at the opening of this Hospital in September, 1947.

His manual dexterity both as an operator and as an amateur carpenter is a lively memory to such few of his colleagues as remain with us.

A more permanent memorial will be his influence on the design of the new Leeds Infirmary buildings, where his architectural ingenuity and untiring work are remembered with gratitude.

His publications include:—

Sarcoma of Iris. *Trans. Ophthal. Soc., U.K.* Vol. XV, p. 814. 1895.

Cysticercus of conjunctiva. *ibid.* Vol. XVI, p. 47. - 1896.

Tumour of optic nerve. *ibid.* p. 139. 1896.

A diagrammatic model intended to assist in the teaching of ocular refraction. *ibid.* Vol. XXI, p. 142. 1901.

A model to illustrate the passage of rays of light through the eye in the various forms of astigmatism. *ibid.* Vol. XXV, p. 307. 1905.

Dr Luckhoff of Cape Town, writes:—

"..... How clearly I can visualise him, his springy alertness, his quickness of mind, his cheerful smile, and the quiet efficiency, equanimity, precision, and finish of everything he undertook.

His handwriting to the last showed the neatness, exactness, and good discipline of an orderly mind.

His complete integrity and openness of character was as refreshing as the nature he loved so well. I have no doubt that he was beloved and admired by all who knew him."

## JOHN ROWAN

JOHN ROWAN died at his home near Prestwick on March 17. A native of Greenock, he retained his love and affection for the West of Scotland throughout his long life. He graduated M.B., C.M., in



H. SECKER WALKER





JOHN ROWAN

*T & R Annan, Glasgow*

the University of Glasgow in 1889, and received his early training in resident appointments in the Greenock Royal Infirmary. He was subsequently a clinical assistant at Moorfields and the Royal Westminster Ophthalmic Hospital. During these formative years, he made friendships which he retained steadfastly, and in his latter years he recalled with a quiet gusto the clinical incidents which had influenced his receptive mind. He made study visits to Berlin, Göttingen, Paris and Dublin, and returned to Glasgow in the early nineties. At that period, F. H. Napier, who now lives in retirement in Johannesburg, succeeded the celebrated J. R. Wolfe, known to several generations of medical students in relation to his method of skin grafting. Rowan became Assistant Surgeon to the Ophthalmic Institution, which had been founded by Wolfe in 1868, and retained this association throughout his life, being promoted Surgeon in 1916 and Honorar Consulting Surgeon in 1924.

He became a Member of the Ophthalmological Society of the United Kingdom in 1893, and was an original member of the Oxford Ophthalmological Congress. He was one of the pioneers of the ophthalmic examination of school children, and data from one of his early papers on the distribution of refractive errors in childhood were incorporated by Karl Pearson in his monograph on the inheritance of vision. Writing did not come easily to him, but he made several contributions to the proceedings of the various clinical and scientific bodies of which he was a member, and his remarks at meetings were frequently pawky and characteristic. In 1900 Rowan was elected a Fellow of the Royal Faculty of Physicians and Surgeons, and served on the board of management of the Glasgow Royal Mental Hospital and the Glasgow Veterinary College. At the meeting of the British Medical Association in 1922, he was vice-president of the Section of Ophthalmology.

He had a love for the country, and devoted much thought and care to the entertainment of his friends on a fishing or shooting expedition. About ten years ago, he retired from active practice, as he found that his progressive deafness was putting too great a strain upon his patients. Both his hospital and private work were carried out with meticulous attention to detail, and in the finest tradition of the great men whom he knew well in the old Moorfields. His manner could be aloof and distant, but once his confidence was gained, the discovery would be made that he was both shy and unassuming. He was for a long time associated with the Royal Sick Children's Hospital, and many old patients can recall his gentleness to them as children.

The present generation of ophthalmologists saw very little of him, and to some he represented the last of the Victorians. Ceremonial and formal they may have been, but we have lost the integration of

outlook and singleness of purpose which were strongly-developed in John Rowan. He was a bachelor, and in the later years he would recall his old friends and teachers; for Nettleship and Treacher Collins he had unbounded admiration. He kept in touch by correspondence with old patients, friends and colleagues up to the end, and his interest in the progress of his chosen specialty did not fail.

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## NOTES

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Honour

SIR STEWART DUKE-ELDER, K.C.V.O., and Mrs. Philippa P. Martin have been elected fellows of University College, London.

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Lectures

PROF. ARNOLD SORSBY will give two lectures on the dystrophies of the retina and choroid at the Royal College of Surgeons of England, on June 24-25, at 5 p.m. each day.

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Pan-American  
Association of  
Ophthalmology

DR. CONRAD BERENS has been elected President of the Pan-American Association of Ophthalmology. The next Congress is to be held in Mexico City in 1952. Twelve vice-presidents have also been elected. Dr. M. E. Alvaro was re-elected Secretary for Countries south of the Isthmus, and Dr. T. D. Allen succeeds Dr. Berens as Secretary for Countries North of the Isthmus of Panama. The Congress held in Havana in January of this year adopted statutes and by-laws, and permanent committees have been set up to deal with encouragement of research, glaucoma, trachoma, lighting and optics, contact lenses, orthoptics, prevention of blindness, neuro-ophthalmology, legal and industrial ophthalmology and other subjects.

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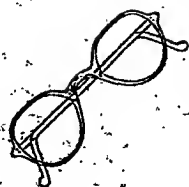
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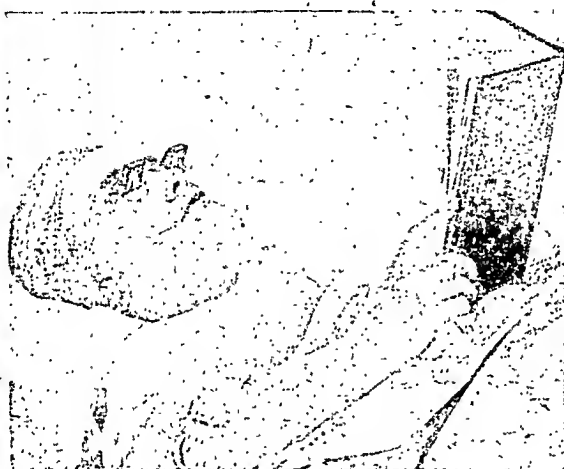
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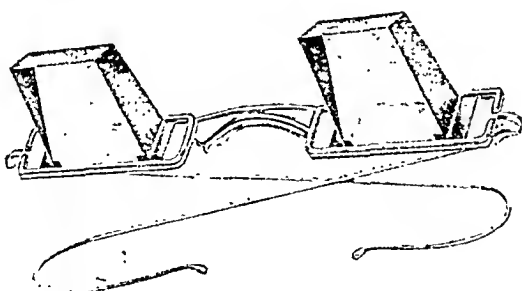
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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

JULY, 1948

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## COMMUNICATIONS

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### DENIG'S OPERATION FOR TRACHOMATOUS PANNUS\*

BY

N. PINES

LONDON

DENIG (1911), operated first in 1910, following the work of Ichikawa, who proved the continuity of trachoma from fornix through the conjunctiva bulbi and so to the cornea. He transplanted first the conjunctiva of the healthy eye, but soon changed to the mucosa of the lip. In the first few years he performed 42 operations with 8 recurrences and failure of the mucosa to heal up on the eye in 5 cases. Ogata in 1930 saw good results from the operation in 95 cases. L. Pines in 1931 reported his results in 406 cases, with no improvement in 42 and recurrences in 16. Since then a considerable literature has arisen about this operation, partly for it, partly against it. The first controversy was about the nature of pannus

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\* Received for publication, January 20, 1948.

itself. There are three theories. The oldest, and, in my opinion hardly tenable, would ascribe the appearance of the pannus to the mechanical action of the infected upper lid, that is to say, the lid rubs the trachoma infection into the cornea. The aetiology of pannus—by continuity or by contact—is still debated. Parsons (1942) is against the continuity and so is Fuchs (1933). Wolff (1944) and Duke-Elder (1938) hold that there is a simultaneous infection of the cornea and conjunctival fornices. Prokrowsky and Taborisky (1914) (Ophthalmological Congress, Moscow, 1913), were partisans of continuity. But between 1911 and 1913 Ichikawa in Japan, Prokowsky and Taborisky in Russia proved the existence of trachomatous follicles in the conjunctiva bulbi and in the cornea itself by microscopical examination. The formation of follicles in the cornea itself was confirmed by many writers. Pasheff (*Klin. Monatsbl. f. Augenheilk.*, p. 361, 1938); R. Huber, *Ibid.*, Vol. LXXI (original article).

How deep do the vessels of the corneal pannus lie? Arkin (*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVII, p. 428, 1926), thinks that there are two forms of pannus—one secondary to the infection of the conjunctiva, and the other a primary infection of the cornea. The blood vessels lie below the membrane of Bowman. All those points must be kept in mind when describing the technique of the operation. The conjunctiva bulbi, under local anaesthesia, is cut starting from the limbus or retreating 0.5 mm. from it towards the periphery making a wound half as wide and as long as the base of the pannus—say from 9 o'clock to 3 o'clock. It is important to cut right through down to the episclera removing all tissues and laying the episclera bare. While an assistant is stopping the considerable haemorrhage by applying swabs with saline and pressing on the wound the surgeon proceeds to cut out and prepare a graft from the mucosa of the lip. Under local anaesthesia a special lip forceps is applied and the graft is cut out slightly longer and wider than the wound of the conjunctiva. The graft is put into warm saline and the wound of the lip is closed by one uninterrupted suture. The surgeon then washes his hands again and while the patient gargles his mouth, the graft is put with the mucosa downwards on a plate of glass or on the hands of the surgeon and the whole of the fat is removed from it so that only the mucosa and submucosa are left.

In my opinion it is not advisable to try and make the graft too thin, but care must be taken not to cut into the graft. Then the graft is put on the wound, mucosa upwards the submucosa downwards on the sclera and is fixed with fine silk to the three sides of the wound, the corneal part remaining free.

It is sometimes advisable, if the wound is too long, to cut the

graft in two portions, cutting at 12 o'clock and readjusting and joining by stitching the two portions. If the cornea is badly ulcerated, the upper part of it may be scraped or cauterised and the graft allowed to cover it. Otherwise the lower part of the graft, if overhanging the cornea, may be trimmed. Sulphonamide powder and sterile vaseline may be put into the operated eye. Binocular dressing for 2-3 days. If the operation is successful, the graft—deadly pale during the operation—will be pink and slightly oedematous when the eye is first dressed. Binocular again. Stitches may be removed after 5 days. The improvement of the eye is usually striking. If the operation is not successful, the whole of the graft or its middle part remains pale, freely movable and is better removed after 5 days. But the eye is still considerably improved. Let us now discuss the different stages of the operation.

Denig used the mucosa of the lip because he believed in this way to present to the trachoma invading the cornea an impenetrable wall of tissue, that cannot be invaded by trachoma as the mucosa of the lip does not possess lymphatic tissue. But the issue is not as simple as that. Why then in unsuccessful cases (one of mine too), is the improvement obtained and maintained for a number of years? Obviously because the trachomatous tissue was cut deeply right to the episclera and so the invasion was interrupted. The trachoma was not very active and the consequent scar of the wound of the conjunctiva remained free from the trachoma. The performed deep peritomy together with the nearly quiescent stage of the trachoma of the conjunctiva (but not of the cornea—obviously a separate stage of the trachoma) would be the explanation, but not the peritomy by itself (only too often failing in cases of active trachoma and pannus). Let me be clear—Denig's operation is suitable only for the third or the fourth stage of trachoma by MacCallan's scheme but no biopsy or clinical examination will be able to gauge the intensity of the still remaining infection.

The surgeon's impression and experience remain decisive. This is why I cannot agree with the opinion of Karlowsky (*Kritishe Bemerkung uber Den. Op., Klin. Monatsbl. f. Augenheilk.*, 1936), or Hallas (*Ibid.*, Vol. LXXXII, p. 401, 1929), that all the benefit of Denig's operation is due to a deep peritomy. Szokolik definitely rejects Denig's operation in favour of a deep peritomy, as proposed by Whitehead in Leeds in October 13, 1922 (*Ibid.*, Vol. LXXVIII, p. 693, 1927). It is safer, therefore, in my opinion, to perform Denig's operation and not the deep peritomy alone. The second point to consider is the interruption not of the course of the infection, but of the toxins only (Kerschmann, *Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVIII, p. 694, 1927). This opinion I think is highly improbable as nobody has yet isolated the toxins of trachoma.



Besides the interruption of the continuity of the trachomatous process, the graft being richly vascularised, improves the nutrition of the cornea. This is quite correct. After 5-10 days the cornea is clear, brilliant and transparent.

Many writers are of the same opinion (Kershman and L. Pines, *Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVII, p. 400, 1926, and Vol. LXXVIII, p. 693, 1927). Kolen (original article, *Ibid.*, Vol. LXXXVII, p. 790, 1931).

But is mucosa of the lip really an impenetrable wall against the invading trachoma? Opinions are sharply divided. Derkach (*Klin. Monatsbl. f. Augenheilk.*, p.409, 1930) saw after Denig's operation that the graft of the mucosa was involved in the trachomatous process as early as 2-3 weeks after operation. In a few weeks time he saw the graft disappear completely in the pannus tissue. He prefers therefore a graft from skin. Ogada (*Ibid.*, Vol. LXXXVII, p.142, 1931) leaves this question of immunity of the graft from trachoma still undecided.

Czukurach (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 262, 1931) made a biopsy of the graft in four cases and saw heavy changes in the epithelium, but the follicles were not typical for trachoma. Ballas (*Ibid.*) found in his histological examination a process very near to trachoma. The same is the opinion of Loewenstein (original article, *Ibid.* p. 390), Seefelder (*Ibid.*, Vol. LXXXI, 1928, original article) saw by microscopical examination trachoma invading the graft of the mucosa. He saw not only follicles, but even the Provazeks bodies in the graft. Similar is the opinion of Tovbin (*Ibid.*, Vol. XCI, 1933). The evidence therefore is very solid and considerable. But a whole phalanx of surgeons are all of a favourable opinion *re* the fate of the graft—it is not invaded by trachoma and forms a protective wall against it.

Such are Denig himself, Kershman, L. Pines (185 operations, *Klin. Monatsbl. f. Augenheilk.* Vol. LXXVIII, p. 694, 1927). Arkin (*Ibid.* p. 428), Endelman (*Ibid.* Vol. LXXV, p. 809, 1925), Budel, who still saw good results two years after Denig's operation, (*Ibid.* Vol. LXXIX, p. 688, 1927), Thies (*Ibid.* Vol. LXXXI, p. 393, 1928), Malkin (*Ibid.* Vol. LXXX, p. 561), Zakas, Blascovitz, Dekers (*Ibid.* Vol. LXXXII, p. 401), Kolen (extensive list of literature). (*Ibid.* Vol. LXXXVII, p. 790), B. Pines (*Ibid.* Vol. LXXXIX, p. 419) *et cetera*. What may be the cause of such a difference? In my opinion, it all depends upon the stage of the inflammation at the time of the operation. Denig's operation is not a panacea for all forms of trachoma of the cornea, but only for an isolated and stubborn pannus when the rest of the process is already quiescent. If it is not, conservative or surgical treatment of the whole affected conjunctiva is necessary before the pannus itself is tackled.

Filatoff and his school look upon the transplantation of the mucosa as a form of irritation or tissue therapy.

They speak favourably of the results of Denig's operations, but for the last few years Filatoff and his school use certain modifications. Besides cutting out a piece of conjunctiva and placing there a free graft of mucosa of the lip, they simply make a hole in the conjunctiva, then undermine it and in so formed corridor they plant a piece of mucosa or a piece of sclera or a piece of cartilage—the results being uniformly very good.

The graft is usually taken from a cadaver and preserved for 4-5 days in the dark at a temperature of 4°.

What is the fate of the graft of the mucosa? Does it remain unaltered, is it replaced by ordinary fibrous tissue or by conjunctiva? This very interesting and rather important question has hardly ever been considered. The surgeons simply were profuse in their laudatory remarks about the suitability of mucosa grafts in the plastic surgery of the eye, but the ultimate fate is usually not discussed.

Thies (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXII, p. 780, 1924) speaks about the reparation of the injured eye and freely uses the mucosa grafts for it, but in his opinion, sooner or later they disappear in the conjunctival tissue. Kershman and L. Pines (*Ibid.* Vol. LXXVII, 1926) simply state that the grafts grew much whiter in colour 12 months after the operation. Budle (*Ibid.* Vol. LXXIX, p. 88, 1927) saw good results in pannus cases operated on by the method of Denig, but he never attempted a microscopical examination of the graft. Gernett (*Ibid.* original article, Vol. LXXXII, p. 230) saw mucosa of the graft still present on the margin of the lid 20 years after the operation, but he did not examine it microscopically. Denig himself (*Ibid.* Vol. LXXXIII, p. 716, 1929) advocates free grafts of mucosa in many torpid inflammations and especially for all injuries of the eye by acid and recommends, if necessary for cosmetic reason, the later removal of the grafts.

Derkach (*Klin. Monatsbl. f. Augenheilk.* p. 409, 1930) saw a graft after Denig's operation disappearing completely in the pannus tissue after a few weeks. Czurrach (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 262, 1931) made a biopsy in four cases in Denig's operation and saw heavy changes in the epithelium. Ballas (*Klin. Monatsbl. f. Augenheilk.*) saw a process very near to trachoma (microscopical examination). Loewenstein (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 390, 1931) thinks that the graft is often invaded by trachoma and becomes assimilated in the surrounding tissues especially in margin plastics of the lid. Ichikawa and Noichesky, as quoted by Kolen (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 790, 1931) think, that the graft of the mucosa cannot be involved in trachoma and no follicles can be formed there,

as no adenoid tissue is present. Kreiker (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVIII, p. 695, 1932) thinks that the grafts disappear after many years, as a result of a chronic inflammatory process and are probably replaced by conjunctiva, but they always disappear.

In the experience of Filatoff and his school the homoplastic grafts of tissues in Denig's operation disappear very quickly, but the conjunctiva less quickly, the mucosa of the lip still less so and the latest of all would be the skin. With the autoplasic tissues, the remnants of the grafts could be seen even 2-3 years after the operation, but in two cases the graft of the mucosa was invaded by a recurrent pannus 2 years 4 months after the operation. The graft was removed and replaced by one of the preserved cadaver conjunctiva. But Scarsky saw the disappearance of the graft of the cadaver mucosa even 30-40 days after the operation.

The above mentioned references are really isolated extracts from rather considerable literature and give a general idea of the prevailing opinion.

Let us now discuss my own cases—not many, but giving a good illustration of the pro's and contra's of Denig's operation.

The first case is that of a woman now 60 years of age, a native from Dwinsk near Vitebsk, in Russia; who arrived here nearly forty years ago with healthy eyes. She caught trachoma here and, in her opinion, it started with a dirty ball hitting her eye, when children were playing in the street near her home. When first seen at the London Jewish Hosp., in 1930-31, she was a case of trachoma cicatricum, third to fourth stage of MacCallan's classification, with partial distichiasis of both lids, especially the lower of the right eye, and pannus, especially of the right eye. A graft of the mucosa of the lip was done on the right lower lid for distichiasis and from 10 to 2 o'clock on the right eyeball for pannus. Both operations were successful, especially that of Denig. Mucosa still can be recognised now, after nearly 9 years.

The second one is that of a man of similar condition, but no distichiasis, only troublesome and recurring pannus. On the right eye Denig's operation was performed 12 years ago from 10 to 12 o'clock. Both ends of the graft took, but the middle part, from 11 to 3 o'clock did not take and started sloughing on the 4th day and on the 6th day I cut it off, leaving the two successful ends intact. The eye remains quiet. The graft at 4 o'clock was removed by me and sent to Mr. E. Wolff for microscopical examination. It still retained all the characteristics of mucosa of the lip 12 years after the operation. On the left eye Denig's operation was performed successfully three years ago and the graft took. The eye remains quiet.

The third case is of exceptional interest. It is a man of over 70 years of age, a native of Kieff, Russia; he was healthy there. In 1915 he emigrated to Berlin and soon afterwards started to suffer from chronic inflammation of both eyes. He arrived here in 1936. In 1943 he presented himself at an ophthalmic hospital in London with an epithelioma of the left upper lid. The epithelioma was removed and he was sent for X-ray therapy. The eyeball became steadily worse. It was a pannus crassus of the cornea, with a thickened and scarified tarsal plate, with a severe inflammation of the whole of the conjunctiva bulbi forming a wall of angry tissue round the cornea, when first seen by me in October 1946. Vis. = counting fingers at 2-4 feet. No conservative treatment being of any use, I decided to perform Denig's operation from 11 to 2 o'clock. The operation took. The vision in 2-3 weeks time improved to 4/60. But when the pannus started to come back, from under the graft new vessels appeared growing into the cornea. Cauterisation did not stop them. Pannus started to grow from all the circumference of the cornea, which became completely vascularised. The Roentgenologist, to whom he was sent for regular inspection, hearing my opinion, that it was probably trachoma gave him 2 sances of radiation. The eye became immediately much more inflamed, the cornea more vascularised and a symblepharon began to form in the internal angle between both lids and the eyeball. It was evident to me then, that it was a mixed process of trachoma, aggravated by X-ray irradiation. The eye is sensitive to X-ray and the inflammation is due chiefly to that. The graft is as vascular and angry, as the rest of the conjunctiva bulbi now a year after the operation. The fate of the eye as far as the sight is concerned, is very dark indeed. In the future lurks the danger of xerosis.

The fourth case is that of a woman of 65 years of age, with trachoma chronicum cicatricum and distichiasis who presented herself in the London Jewish Hospital 19 years ago with a tremendous serpiginous ulcer of the right eye and chronic dacryocystitis. The lacrimal sac was removed, and the eye, but not the eye-sight, was saved by a large graft of the mucosa of the lip, from 10 o'clock to 2 o'clock, right across the cornea and sufficiently wide to cover the ulcer. The ulcer healed up with a huge leucoma and after 7 days the middle part of the graft was removed, leaving the well ingrown ends of the bridge intact. The 4 o'clock end was removed and sent to Mr. E. Wolff for microscopical examination. It is still mucosa of the lip 19 years after the grafting.

If the characteristic part of trachoma is the scarring and shrinkage of the conjunctiva, then it is advisable to use the graft of the mucosa as frequently as possible in any plastic operation on a trachomatous eye, as it is excellently tolerated by the eye and increases the shrunken conjunctival surface.

I was defeated only in one series of cases. In 1917, when in charge of an eye department on the front of the Russian Army, I had many cases of trachoma where the chief feature was the mucous degeneration of the upper fornix, the cornea and tarsal plate being only slightly affected. I excised the fornix only and grafted on the wound a strip of the mucosa of the lip. It took on, but in 50% of my patients it produced a leucoma of the upper part of the cornea. I stopped the grafting and simply excised the fornix and never had any leucomata afterwards.

### Summary

1. Denig's operation is highly advisable in cases of isolated pannus and quiescent trachoma of the lids and bulbi. Any active trachomatous focus must be destroyed first.

2. Mucosa of the lip, if grafted on the eye in these conditions remains unchanged for many years.

3. More frequent use of mucosa grafts is advocated for any plastic operation of the trachomatous eye.

### Case Reports

Mr. A. S., aged 54 years. Both eyes trachoma chronicum cicatricum. Right eye, Denig's operation 12 years ago (1935).

The middle part of the graft did not take. The end of the graft at 3 o'clock was removed and sent for investigation.

Special thanks are due to Mr. Eugene Wolff, F.R.C.S., and to Mr. W. H. Gordon, Assistant Pathologist to Royal Westminster Ophthalmic Hospital, who kindly examined the specimen and reported.

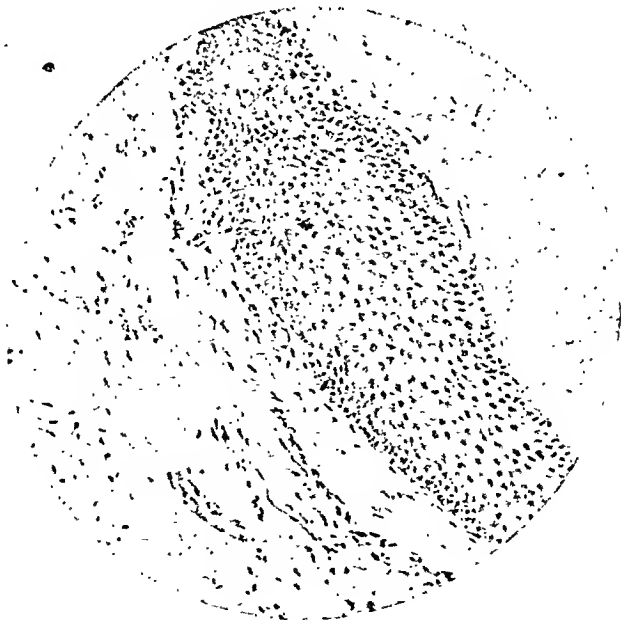


FIG. 1.

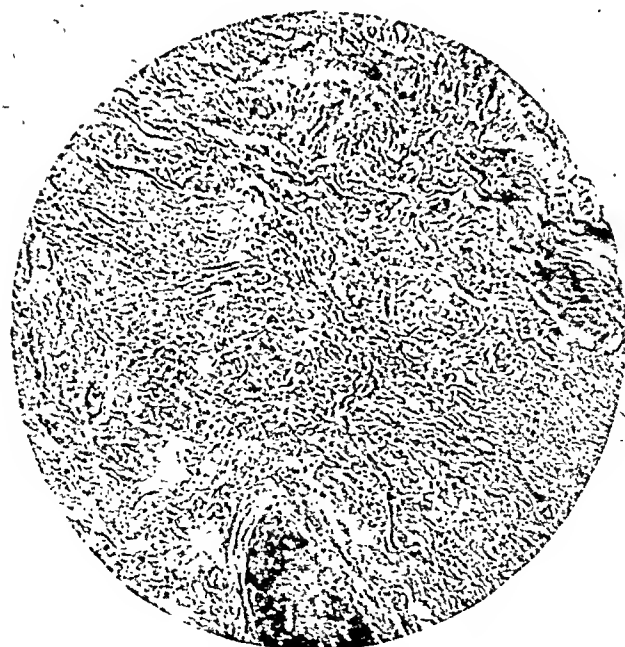
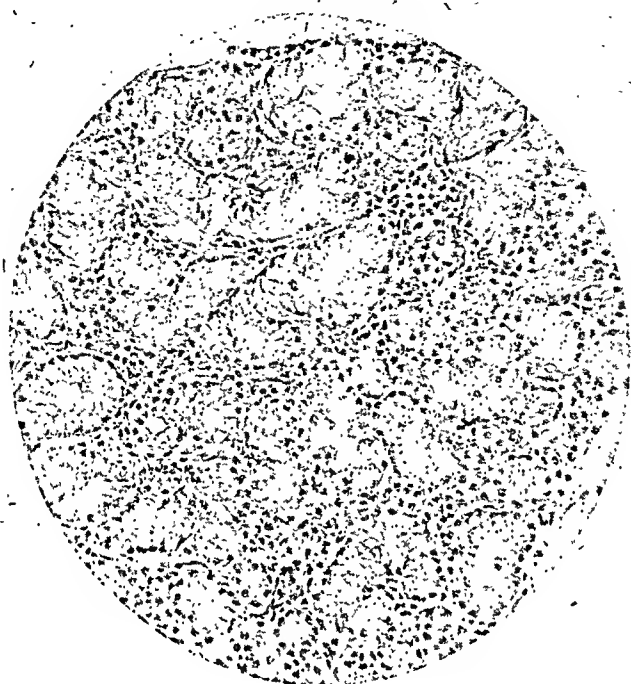


FIG. 2.

The following is their report:—

The epithelium throughout the section is stratified, squamous, without cornification. It is not of uniform thickness, being much thicker over about half the section at one end than over the remainder, and the thicker half shows slight oedema of the prickle-cell layers (acanthosis). The papillae are stunted for the most part, though in the area of thin epithelium there are one or two considerable downgrowths of epithelium, which, however, remains quite regular in arrangement. The immediate subepithelial connective tissue is fairly close-fibred and in only one place (in the thick epithelium area) is there slight round-celled infiltration. The deeper connective tissue is looser and vascular.

The characters of the whole graft, therefore, are those of mucous membrane, slightly modified by stunting of the papillae, and in part, by acanthosis.

Female, aged 60 years. Both eyes trachoma chronic cicatricum. Right eye, serpiginous ulcer 19 years ago. Healed by graft of the mucosa of the lip.

Report of examination of biopsy specimen.

The specimen consists of connective tissue and its covering of stratified squamous epithelium.

The epithelium, 8 or 9 cells thick shows:—

- (i) Basal cells, which are cubical or low columnar, whose oval nuclei stain moderately with haematoxylin, and contain a few deeply-staining chromatin particles.
- (ii) Intermediate polyhedral cells between which are cell-bridges.
- (iii) Surface cells which are flattened but not keratinised.
- (iv) Adventitious cells—an occasional polymorphonuclear leucocyte.

The outline of the deep surface of the epithelium is somewhat undulating, presumably representing the succession of imperfectly formed papillae and inter-papillary downgrowths.

In addition there are seen in the sections two epithelial downgrowths, a small solid one extending horizontally just below the epithelium, whereas the other, which has a hollow cavity, extends vertically to the surface for a distance equal to three or four times the thickness of the usual epithelial layer.

The subepithelial tissue consists of loose connective tissue, appearing somewhat oedematous in places, and well supplied with blood and lymphatic capillaries. Just below the epithelium it is infiltrated with lymphocytes and plasma cells in considerable numbers, together with some endothelioid cells. Situated also in this tissue are a few tubulo-racemose glands, whose acini are lined by columnar cells with nuclei near the cell-base, whilst an outer cell-layer is formed of darker small cubical cells. These glands resemble buccal glands.

*Opinion.* In the specimen the structure of the original mucous membrane graft is maintained both in its epithelial and subepithelial parts.

My most sincere thanks are due to Mr. E. Wolff and Mr. W. H. Gordon for their invaluable co-operation in preparing, examining and reporting on two pathological specimens of mine.

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## HYDATID OF THE ORBIT

BY

SIR HENRY HOLLAND, C.I.E.

INDIA

TEXT-BOOKS have very little to say regarding this condition. Fuchs merely mentions that cysts formed by the entozoa echinococcus and the cysticercus variety are found in the orbit. Duke-Elder states that these are not very rare in the orbit, although extremely rare intra-ocularly. Parsons contents himself with the statement that hydatid tumours are rare in England. Elliot's *Tropical Ophthalmology* treats the subject in some detail. He points out that it is common in the Argentine. Cabaut estimated that one in every 4,714 eye patients were cases of echinococcus of the orbit. This also refers to the Argentine. Demaria of Buenos Aires has also written on the subject in the *Arch. d'Ophthal.* on November, 1916, while Cabaut's paper was published on February 25, 1904. He wrote stating that though these cysts may develop in any part of the orbital cavity, they generally lie in or about the muscular cone, and he had never seen a case either within the optic nerve or within the eyeball.

My experience of this condition (eight cases) bears out Cabaut's findings. Those cysts that I have seen are generally on the nasal side, and always in the upper fornix. I have also had the same experience as Demaria regarding the absence of any pericystic membrane in any of the cases. Seldom has pain been a predominant feature of this disease, and in some cases it has been entirely absent. The proptosis varies according to the duration of the condition. In the early stages there is only some fullness of the upper fornix while in the later stages the proptosis assumes such large proportions that the patient cannot close the eye, and there is often eversion of the lower lid, well marked chemosis, and occasionally ulceration of the cornea. Vision is in most cases excellent and I have seen in two cases almost normal vision although the patient could not close the eye owing to the proptosis.

The cystic swelling requires to be differentiated from several other conditions, the most common being dermoid cyst and the varieties of exophthalmic ophthalmoplegia. The cystic swelling is for all practical purposes unilateral. The diagnosis may be clinched by aspirating the tumour and microscopic examination of the contents after the patient has been prepared for operation. If the typical hooklets are seen, the needle should be left in place and the cyst excised forthwith.

The treatment consists in removal of the cyst, entire if possible. This is an extremely difficult procedure owing to the friability of the



cyst wall, and in these eight cases I have succeeded only once and my son, R. W. B. Holland has succeeded once. An incision is made into the conjunctival fornix nearest the tumour. The muscles are not usually divided, and blunt dissection enables the operator to display the bluish white cystic tumour. The contents are then aspirated, and with the needle still in place one half the volume of 20 per cent. formaldehyde is re-injected. An attempt is then made to remove the cyst entire with a pair of fixation forceps. If it tears, however, recourse must be made to a piecemeal removal. The cyst wall has often a very deep attachment, in which case it is difficult to be sure that the whole of the cyst wall has been removed.

The final result of the operation depends on whether the cyst has been removed in its entirety or not. Failing this, mild sepsis and a severe reactionary swelling and chemosis are apt to follow, even though the wound is drained with a fine rubberglove drain as a routine. The vision of the two patients, whose cysts were removed entire, was unimpaired. It is impossible to give an opinion of the ultimate visual result of the other six patients, because they did not report again to hospital after being discharged two or three weeks after the operation.

From this series of cases it is evident that the earlier the patient comes for treatment the better, since operative removal of a large cyst is rendered very much more difficult.

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## A LOW POWER INFRA-RED MICROSCOPE

BY

T. STUART-BLACK KELLY

MANCHESTER

A DESCRIPTION has been given of the application of an infra-red viewing system to the penetration of corneal opacities<sup>1</sup>. The basis of the device is a German image converter tube that has the property of transforming an image in the infra-red region of the spectrum (at about 10,000 A.U.) into a visible image on a fluorescent screen. Through the courtesy of the Admiralty Research Laboratory we have been able to carry out a similar investigation using the equivalent British instrument. It has been confirmed that such equipment can be used with advantage when assessing the advisability of a corneal graft in certain cases.

*Apparatus.* The instrument in its present form was originally designed for an investigation of the variation of pupil diameter at very low levels of illumination. The viewing device, which can

replace the normal binocular microscope on a slit-lamp table, consists of a low power microscope incorporating an infra-red image converter tube<sup>2</sup>. The latter is a small glass tube containing an infra-red sensitive photo-surface and a fluorescent screen. An infra-red image focused on the former is transformed into a visible image (green) on the latter. A high voltage (6,500 volts) is necessary to actuate the converter and this is supplied from a vibrator power unit operating from a 12 volt-battery. The microscope can be mounted on the normal binocular stand using a simple-adaptor. Overall dimensions of the instrument are 16"  $\times$  2½" diameter. Varying layers of filter, absorbing visible light but transmitting the infra-red, are fitted over the slit-lamp.

*Application.* The improved transmission characteristics through a small particle scattering medium of the longer wave-lengths of radiation results in improved visibility through certain types of corneal opacity using the infra-red microscope. Experience has been limited, but results have shown that considerable density of cornea can be penetrated by suitable angles of projection and degrees of purity of beam. A contact glass improves penetration of a rough surface. A Koeppe glass could be tried for retina or vitreous. After-cataract penetration varies with the purity of beam. Penetration of cataract appears to depend on the chemistry of cataract, not the apparent density, *e.g.*, if in an opaque cornea the active iris dilates, well revealing apparently a clear lens, the lens may or may not have a secondary or senile cataract. Early normally invisible calcification appears to show a strong fluorescence.

Possibilities are apparent in pathological and clinical investigations. The instrument is easy to use and even less trouble to the patient than the visible slit-lamp arrangement.

*Availability.* The image converter tubes have now been made available commercially and, in addition, the Admiralty are prepared to receive enquiries regarding the assembly of complete microscopes for use in clinics. Any such enquiries should be addressed to the Director of Research Programmes and Planning, Admiralty, Fanum House, Leicester Square, London, W.C.2.

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## XERODERMA PIGMENTOSUM WITH AFFECTION OF THE EYE\*

BY

JOHAN SÆBØ

NORWAY

IN the present article an account is given of a skin disease with ocular manifestations. At the beginning the skin disease was diagnosed as lentigenes and the eye-affection was suggested to be a melanoma bulbi. Observation of the clinical picture, however, and later familial investigations, gave clear evidence of a close connection between the two affections, and the condition became recognised as xeroderma pigmentosum (x.p.).

X.p. belongs to the so-called actinic dermatoses, and is a rare disease in this part of the world. From the present work it clearly appears that in the initial stage of the disease the diagnosis may be difficult. Here the condition has been described from its first manifestation up to the fully developed clinical picture.

The term lentigenes has been made to describe from pinhead to lentil-seed-sized, brownish maculae, considerably darker than freckles. They may be sitting close together or singly, and so they may be scattered all over the body. They are not congenital, but appear in the growing age. Lentigenes, in contrast to ephelides, are fairly uninfluenced by light.

A melanoma is, according to G. Miescher, a new-growth having the power of forming melanin. There are malignant and benign forms of these tumours. Distinction is further made between epidermogenic and cutaneous forms and those proceeding from the mucous membranes. Examples of epidermogenic melanomas are naevi spili, ephelides and lentigenes. "Mongolenfleck" and "Der blaue Naevus" (Jadassohn) are cutaneous forms.

Melanomas also occur on the eye, and seem to have three sites of predilection: the corneal limbus, the lacrimal caruncle and the palpebral border. They may be malignant or benign. A benign melanoma may suddenly become malignant, and in these conditions it has been claimed that external factors (traumas) are of some importance in the transition to malignancy.

Schieck declares that the suspicion of malignancy should be specially strong where a macula suddenly begins to grow in an individual past the age of 30 years. Special attention should also be paid to tumours presenting marked pigmentary irregularities or

\* From the Ophthalmological Clinic of the University Hospital, Oslo. Chief: Professor Birger Malling, M.D. Received for publication, January 29, 1948.

unusually strong pigmentation. The case is a clear one where the tumour infiltrates a considerable part of the conjunctiva, and particularly in the presence of "Abklatsch-metastase," which is no rare occurrence. In these forms of newgrowths, other metastases are comparatively rare.

After this introduction, three cases of x.p. with ocular manifestations will be recorded.

### Case report

Case I. M.L., a woman aged 17 years. Previously, she always had been in good health, apart from having "freckles" on her face, neck, arms and legs. As far as she could remember, the spots on her skin had always been there, but had presumably increased in size and number during the last years. In summer they caused some discomfort, as she was sensitive to sunlight and apt to become sunburnt. In the last years she had suffered from photophobia.

The patient had for several years had a dark spot in her right eye. Possibly it had lately grown somewhat larger. It had given no trouble, but now she wished to have it removed, mostly for cosmetic reasons.

The tumour was situated at the outer limbus of the right eye, extending about 3 mm. into the cornea. As in pterygium a conjunctival fold was drawn after it. The tumour showed marked brownish pigmentation, but otherwise it resembled an ordinary pterygium. (To mention now that the appearance of the tumour was the same as that of a newgrowth developing several years later at the inner limbus of the same eye, is anticipating the sequence of events. See Fig. 8, Plate II.)

The location of the tumour at the temporal limbus may seem surprising. However, from the literature it is seen that whereas some authors insist that a pterygium is always situated on the nasal side others also claim the temporal side as a possible location. The brownish colour of the tumour was thought to have some connection with the otherwise hyperpigmentary condition of the patient.

The tumour was removed in the usual way, and on examination 2 months after excision, everything seemed normal. However, examination 2 years later, revealed a recurrence of the tumour. This is seen in Fig. 4, Plate II. A semilunar-shaped tumour was seen at the temporal limbus. At its widest it was about 4 mm. and extended over half of the corneal circumference, from "6 to 12 o'clock." The essential part of the tumour was lying in the cornea. The outward transition from the conjunctiva was even. Prominence was about 1.5-2 mm., and it terminated in a greyish-brown wedge

under and into the corneal epithelium. In the middle there was a cystic bulging, greyish-brown and with some darker parts. It was richly vascularized, moderately hard and not movable against the underlying tissue. No ulceration was present. A slit-lamp examination revealed the inner border of the tumour as a greyish-brown wedge, corresponding to Bowman's membrane. There was a strong admixture of brown pigment, and brown pigment-dust was seen in the cornea beyond the tumour proper. Otherwise the right eye appeared to be normal. No pathological changes in the left eye. Visual acuity: 5/10 o.dext., 5/5 o.sin.

This patient, accordingly, presented a dark brown, unevenly pigmented tumour at the corneal limbus, evidently a recurrence after the tumour removed 2 years earlier, which seemed to be steadily invading the cornea. Appearance and course indicated malignancy and the probability of melanomalignoma.

The patient was admitted to the Ophthalmological Clinic of the University Hospital, Oslo, for observation and treatment. The report of her eye-condition from this clinic corresponds to the description above. W.R., v. Pirquet negative. Sedimentation rate 5 mm. The patient was examined at the Dermatological Clinic of the University Hospital with the following result: "The skin over the face, the neck, and to less degree over the extremities shows pronounced lentigenes. This skin condition represents a special form of pigment-naevi and defies treatment. It is reasonable to see her melanoma at the corneal limbus in relation hereto." In connection with this description, reference is made to Fig. 2, Plate I, and Fig. 7, Plate II, clearly illustrating the changes in the skin. In Fig. 1, Plate I, the skin-condition is specially distinctive.

Before proceeding to discuss the therapy for the eye-affection in this special case, it may be justifiable to make some comments on the treatment of melanomas in general.

The treatment of benign melanomas or naevi pigmentosi is essentially of cosmetic nature. For fear of malignancy some authors recommend the removal of any naevus. This may be slightly exaggerating the danger. But naevi occurring at an advanced age and showing irregular or very strong pigmentation, and particularly when growth commences after repeated irritation should be removed. Excision in normal tissue is recommended in flat, scarcely infiltrated growths. Electro-coagulation is also considered effective in such cases, whereas X-ray treatment is of no use.

In melanomalignomas excision has gone somewhat into the background. X-ray and radium treatment, electrolysis and diathermo-coagulation being preferred. The two latter methods

PLATE I



FIG. 1.

Xeroderma pigmentosum. Skin condition.  
Tumour at the limbus. Case I, M.L.,  
aged 19 years.



FIG. 2.

Xeroderma pigmentosum. Case 1,  
M.L., aged 19 years.



FIG. 3.

Xeroderma pigmentosum. Case 2,  
A.L., aged 32 years.



FIG. 4.

Xeroderma pigmentosum. Tumour at the limbus. Case 1, M.L., aged 19 years.



FIG. 7.

Xeroderma pigmentosum. Malignant tumour on the skin of the jaw. Case 1; M.L., aged 25 years.



FIG. 5.

The same tumour two months after treatment with X-rays.



FIG. 8.

New tumour of the inner limbus. Case 1, M.L., aged 27 years.



FIG. 6.

The same eye four months after treatment.



FIG. 9.

Xeroderma pigmentosum. The shoulder region. X: malignant new growth. Case 2, A.L.



FIG. 10.

Xeroderma pigmentosum. Case 3, A.G., aged 18 years. 1, Whitish tumour at limbus. 2, Tumour corneal. 3, Carcinoma cutis.





are considered the safest. Lately, however, this conception has been revised in favour of the X-ray-radium treatment. Evans and Leucutica (1931) treated 21 growing naevi, possibly already malignant, *i.e.*, of a nature similar to the one described here, with massive X-ray doses, with excellent results in all cases.

It is possible, as mentioned above, that our case of melanoma bulbi should be regarded as a melanomalignoma. The excision of a piece of tissue for diagnostic purposes might have been desirable, but was hardly advisable. At the clinic there was some hesitation before the choice of therapy, and enucleation was discussed. However, it was decided to try X-ray treatment before resorting to this radical intervention. In the course of 29/9-21/10, 1938, the patient received a total of 4,000 r: single doses of 200 r. The eye was irradiated tangentially and laterally. The field of irradiation was limited by glass tubes and the skin protected by lead rubber.

Distinct hyperaemia developed during the treatment. In the course of one month, the tumour commenced to subside. About 2 months after institution of the treatment the tumour had nearly disappeared. This clearly appears from Fig. 5, Plate II, showing some pigmented spots at the site of the tumour. After another 2 months practically all traces of the tumour had vanished, see Fig. 6, Plate II. The corneo-scleral border was somewhat blurred, and dilatation of an episcleral vessel was noticed. Slit-lamp examination revealed some fine vascular shadows in the cornea and some fine brown dust in the epithelium. Otherwise the eye appeared normal. Visual acuity 5/5.

The patient accordingly showed no recurrence during 3 years of observation. The illustrations clearly show the effectivity of the local X-ray treatment of the tumour. It might, therefore, be of some interest to our colleagues, meeting similar cases, to note doses and mode of application.

At this time the condition was believed to represent a melanomalignoma bulbi, intimately connected with the lentigenes of the skin. Later investigations proved the correctness of this connection, but on a basis different from what had been presumed. Complications from the skin, and not least some familial investigations that were made, proved the fundamental disease to be xeroderma pigmentosum.

About 8 years after the removal of the first "pterygium" (the patient now aged 25 years), a pea-sized tumour developed on her right cheek, see Fig. 7, Plate II. Ulceration started in the centre of the tumour, and the ulcer could not be made to heal in spite of treatment. The patient was referred to the Roentgen-Radium Institute of the University Hospital with the diagnosis: carcinoma

basocellulare. The following is seen from her chart: "On right cheek, somewhat above the mandibular margin, there is an oval ulceration, somewhat larger than a pea, with elevated borders and a central part covered with a crust." Biopsy proved: carcinoma basocellulare.

The patient received radium treatment. Tube preparation: 2 tubes of 5 mgm. RaE. Filter: 0.5 mm. platinum. Radium-skin-distance: 5 mm. Intensity in r. per hour: 66.5 for 54 hours = 3.600 r.

The result of treatment was good, only a whitish scar being left 4 months later.

At this time the patient observed another tumour on her neck at the insertion of the sternocleidomastoid muscle. The tumour was the size of a hazel-nut, was hard and non-sensitive. Biopsy was made and the diagnosis read: carcinoma with regressive changes. The patient was treated with radium: 3 radium needles of 5 mgm. RaE. Filter: 1 mm. platinum. Intubation for 42 hours. The result was good. But already a few weeks later a gland, the size of the kernel of a nut, developed in the fossa supraclavicularis on the same side, slightly lateral to the treated area. The gland was extirpated and examined: little differentiated carcinoma.

Later the patient has been treated at the Norwegian Radium Hospital, Oslo, for similar tumours of the skin. Here she has received treatment with X-ray, and the effectivity has always been good. At the present time she has an ulcer on the back of her hand consequent to radium-treatment of a tumour in this place. Otherwise her general condition was good, and she was continuing her usual work. She was now 27 years old. On renewed examination her left eye was still seen to be normal. But at the nasal limbus of her right eye there was a dark spot, similar to the "pterygium" that was removed 10 years earlier, see Fig. 8, Plate II. There was a triangular brownish area, reaching from the limbus and about 3 mm. into the cornea. As in pterygium, a fine conjunctival fold is stretching toward the spot. In slit-lamp examination the spot was seen to consist of fine pigment-particles, situated in the epithelium. Otherwise the eye was normal. Visual acuity 5/5.

On questioning the patient about her family it was learned that her brother is suffering from a similar disease. He has also been examined.

Case 2. A.L., a man aged 32 years. As long as he can remember, he has had brown spots on his face, neck and extremities, similar to those seen in his sister. (See Fig. 3, Plate I.) They had grown somewhat larger and darker in the course of

years. He was very sensitive to sun-light and easily became sun-burnt. At times he suffered from photophobia. The above mentioned parts were thickly covered with irregular brown maculae, from pin-head to lentil-seed size. In some places the spots were flowing together into larger irregular fields, as on the right cheek and on the forehead. These parts were brownish-black. A great part of the maculae resembled freckles. The skin over these parts was atrophic with numerous cicatricial spots. Fig. 9, Plate II shows the region of the shoulder, with a little malignant new-growth. The changes in the skin were identical with those of his sister.

At the age of about 27 years a tumour developed on his neck and was effectively treated with X-ray. Some time later an ulcer on his left ear was healed by radium treatment. Since then new ulcers or tumours often have appeared on his eyebrow, cheeks, on his forehead, at the root of his hair (Fig. 3, Plate I), and on his arm. X-ray or radium treatment has been given with good result. Otherwise the patient was feeling well and had been working most of the time.

At the Norwegian Radium Hospital these new-growths had also been interpreted as malignant naevus-cell tumours, developed on basis of x.p.

On examination of the patient's eyes, changes were found, that must undoubtedly be connected with the skin-disease.

O.dext. Close to limbus, corresponding to "9 o'clock," a small, distinctly red spot in the conjunctiva was seen, about 2 mm. in diameter. On slit-lamp examination it was seen to consist of a number of local dilatations of episcleral vessels. The vascular spot had been noticed for years by the patient. Otherwise the eye was normal. Visual acuity 5/5.

Familial Examination gave the following result (see p. 404).

1st generation. Photographs of the two, who died at an old age, showed normal pigmentation of the skin.

2nd generation. Photographs of all these, who also died old (aged 76, 90, 83, 76 years), showed normal colours of the skin.

3rd generation. These two were first cousins, and were now 58 and 57 years old. They had both normal skin-pigmentation.

4th generation. This includes 7 children in a marriage between first cousins. No. 3 is the patient A.L., and No. 5 the patient M.L. As to No. 4, K.L. (29 years old) there was some doubt. On her face, especially on the nose and proximal parts of the cheeks, there were some brownish spots resembling those seen in the two patients. The rest of her body showed normal pigmentation of the skin. The brownish spots were not distinctly differentiable from

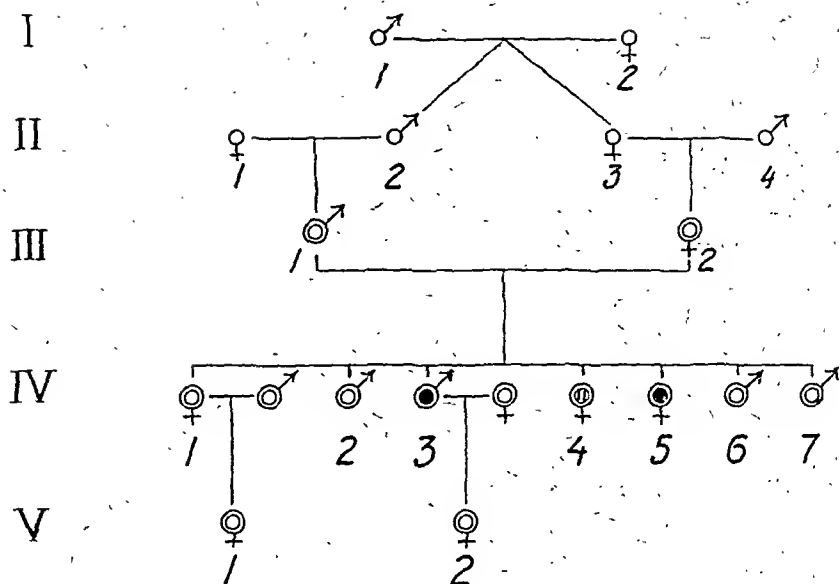


FIG. 1.

Pedigree demonstrating the consanguinity of the parents of the patients affected with xeroderma pigmentosum. (Gen. IV: No. 3: A.L., No. 4: K.L., No. 5: M.L.)

○ Examined,    ⊗ Affected,    ○ Probably affected.

ordinary freckles, but with our present knowledge of the disease in her family, the spots will naturally be suspected to be of the same character. Nos. 1, 2, 6 and 7 from 4th generation had normal skin pigmentation. The youngest one was 20 years old. No. 1 had a husband to whom there was no blood relationship, and these had one child (2 years old). Both of them had normal skin-pigmentation. No. 2 was unmarried, and so were Nos. 4, 5, 6 and 7. No. 3, the patient A.L., was married to a woman to whom there was no blood relationship. She and their 2 years old child seem as yet to be normal.

The familial incidence suggested that the disease was hereditary, and in all probability due to a recessive gene. The fact, that the affected individuals occurred in a consanguineous marriage was a strong indication thereof. This conception is in accordance with earlier results. Thus Bering and Barnewitz: *Handbuch der Haut- und Geschlechtskrankheiten* (1932), found that 17.1 per cent. of the affected individuals occurred in consanguineous marriages. This view is shared by Karl Zieher in his: *Lehrbuch und Atlas der Haut- und Geschlechtskrankheiten* (1928).

Ingolf Schiøtz, M.D., Oslo, has most kindly brought to my notice that a patient suffering from x.p. and affections of the eyes was at the Dermatological Clinic of the University Hospital in Oslo in 1920. Detailed information about the patient has been obtained from this source.

Case 3. A.G., male. His journal informs us that he was examined by an ophthalmologist at the age of 10, and that a whitish blister as big as a pin-head had been present at the inner corneal limbus of the left eye for a period of about a year. This blister had slightly increased in size. The examination gave the following results:

Left eye. There is congestion of the conjunctival and episcleral vessels of the inner part of the eye. At the inner corneo-scleral limbus there is a bluish-white, hard, insensitive, cauliflowerlike tumour, about 1-2 mm. in over the cornea. The eye is otherwise normal. Visual acuity 5/6.

Right eye is normal.

The ophthalmologist considered the tumour at that time as benign, but wished to excise it all the same. This was not done, however, and the patient was lost sight of until he was 18 years old. The clinical picture was then quite changed, and the patient was sent to the Dermatological Clinic of the University Hospital, Oslo. Here he stated that the above-mentioned tumour, in the course of the last seven years, had grown to cover the whole eye, which became almost blind at the age of 16 years. The patient further stated that at the age of 9-10 years, the skin of his face had become uneven in places, and that at times the lumps had become sores. Some years later, the lid borders of both eyes became sore. His condition grew worse during the summer.

The Dermatological Clinic of the University Hospital, Oslo, gave the following description of the case (17/3/1920). See Fig. 10, Plate II. Large and small telangiectases, angiomas and naevi are now visible in the face, on the chin, the neck, the nose and less marked on the forehead. These naevi are raised above the level of the skin, and have a yellow, wart-like surface. This is especially marked on the left lower lid and on the ear. Between these telangiectases and angiomas, small scar-like atrophies are visible. The lower lid is sore and cracked and has numerous telangiectases. On the left lower lid, there is to be seen a crust-covered ulceration, limited by a clearly infiltrated zone.

The patient was examined at the Ophthalmological Clinic of the University Hospital, with the following result: The extraordinary eye disease presented by A.G. has not hitherto been "seen at the clinic. His disease must be considered a malign-tumour-like new-

growth, epithelioma corneae, perhaps originating in the limbus corneae."

Left eye. Below the external canthus, there are some crust-covered uneven sores. The edges of the lids are thick and red with sores and crusts. The conjunctival vessels are moderately congested. Numerous blood vessels are visible in the conjunctiva and these invade the cornea. Together with the neighbouring parts of the sclera, the cornea forms a kind of proliferating tumour-like mass, with an uneven, partly rough surface, greyish-red in colour. This mass seems to form a thin shell about 2 mm. thick which covers cornea and the nearest parts of sclera to an extent ca. 15 mm. in diameter. Visual acuity: Hand movements at  $\frac{1}{2}$  m. Light projection good.

Right eye. The lid borders are thick and partly covered with crusts. On the upper eyelid can be seen a dark "wart" ca. 2 mm. in diameter. The conjunctival vessels are congested. At the outer corneo-scleral limbus, there is a small whitish pinguecula-like condition and a fair number of vessels invade this. Visual acuity: 5/5. At the beginning of his stay in hospital, the patient was given a light cure, and his condition became clearly worse during this time. Later on, he was treated with epilation, mercury oxide ointment and silver nitrate, without any certain effect.

As the process was advancing in the left eye, enucleation was advised. However, he refused to undergo the operation, and returned to his home after a stay of 1½ months.

During his stay in hospital, excision of a piece of tissue from the ulcer on the left inferior palpebra was excised for microscopical examination. The diagnosis was carcinoma.

At our request the clergyman in his home district has told us his later history as follows: One year after his return home, the left eye had to be excised because of the pain it gave him. After a second year, the right eye had to be excised for the same reason. The malignant new growths spread gradually over the whole face, so that he became quite disfigured and he died at the age of 21 years.

Familial investigations in this case gave no result of special interest. The patient was the illegitimate son of parents who are now both dead. No consanguinity between the parents.

### Discussion

Here the disease xeroderma pigmentosum has been followed from so early a stage as to defy certain recognition on a basis of the findings in evidence, and up to the fully developed clinical picture with serious complications. When additionally, as in cases 1 and

2, the recessive mode of heredity must be considered established, the diagnosis must be correct.

In one of the above mentioned cases, malignancy was first evidenced in a tumour of the eye. If malignancy had proceeded from the pigmented spots on the skin, the diagnosis might have been established at an earlier stage.

X.p. is a rare disease in this country. In 1939, Professor Danbolt of Oslo demonstrated such a case at the Norwegian Dermatological Society. The disease is more frequent in southern countries. (See Junes's work from Tunisia.)

The disease is congenital and develops under the influence of light in the course of the first years of life. According to Bering and Barnewitz, different stages are recognisable: 1, Hyperaemic-inflammatory stage; 2, stage of brown warts and excrescences; 3, formation of malignant growths.

The disease often includes ocular manifestations. Ectropion may be seen subsequent to palpebral affections, pigmented conjunctival tumours and teleangiectases. Papillomas are occasionally seen at limbus corneae and in the cornea proper. The nature of these occurrences is often malignant, and they will propagate to other parts of the eye, with resulting blindness.

As a rule x.p. is a serious disease, and the patients often die at an early age. However, the course may be protracted over years and decades, but the prognosis is always grave.

In the two cases first described, the course of the disease seems fairly protracted. Its serious character, however, is seen from the frequent formation of malignant new-growths, and from the metastasis to a gland in the patient M.L., case 1.

In the two patients, cases 1 and 2, the disease became manifest at a comparatively advanced age, and this may agree with the relative benignity in these cases. Literature shows that the earlier the manifestation of the disease, the greater the malignancy.

As seen from the first two cases of x.p., local X-ray and radium treatment gave an excellent effect. Accordingly it is important to detect the malignant new-growths at an early stage in order to get them treated before they spread to other parts of the body. The constant re-appearance of malignant new-growths both in the eyes and in different places in the skin was arrested by this treatment in its deleterious activity. After surveying the course of the disease, we can now assume that malignancy was already present at the age of 17 in case 1, and of 27 in case 2. These patients are now aged 27 and 32 respectively and continue in good health and are doing full-time work.

Case 3 is well suited for a comparison from this point of view



with the two mentioned above, as the clinical course seems to have been similar. The correct and serious nature of the disease was overlooked in both cases 1 and 3, as both of them started with relatively innocent looking tumours in the eyes and even the changes in the skin showed so few of the characteristics of the disease during the first years that they did not give sufficient grounds for an x.p.-diagnosis.

In case 1, a pterygium-like tumour developed in the right eye from the age of 15 years. The pigmented spots in the skin were thought to be freckles. A tumour in the eye was excised when the patient was 17, but already at the age of 19 years she had a certain relapse. This was taken to be a melano-malignoma. Also then the pigmented spots in the skin were understood to be lentigenes. Not until the patient was 25 years old the constantly re-appearing of malignant new-growths in the skin had been proved malignant by microscopical examination, and the disease was finally diagnosed as x.p. Proof of recessivity further supported this diagnosis.

In case 3 a tumour at the inner limbus of the left eye was found at the age of ten. The tumour was whitish and was first taken to be benign, and not considered in the conjunction with the other symptoms from the patient's skin. It was only when the patient was 18 years old that the malignancy of the tumour and its real nature were understood, and also in this case, in connection with closer examinations of malignant new-growths in the skin. The tumour in the eye had now spread over the whole cornea and neighbouring parts of sclera. At the age of 16 years, the eye was nearly blind. There was now a little whitish tumour at the limbus corneae of the right eye. This spread over the right eye in the same fashion until that eye also became blind. Both eyes had to be excised. Later on, malignant new-growths spread over the whole face, and the patient died aged 21 years.

Thus we see that after a relatively quiet period from 10-18 years of age, with changes in the eye which were considered relatively harmless, the disease took an exceedingly malignant course. In this case, too, there was now no doubt that the fundamental disease was x.p.

If we now compare the results of the treatment of these three cases, which were very much alike in their clinical course before treatment started, the question naturally arises: Could the development of malignant new-growths have been stopped by early applied X-ray or radium treatment also in this third case?

As already mentioned, these three cases show that the diagnosis x.p. may be difficult in the early stages of the disease, which is rare in our country. This is also in agreement with the declaration

from the Eye Clinic at the University Hospital, where it has been stated that no case of this strange eye disease had yet been seen there.

There is reason for supposing that the course of the disease in our country is less rapid than we usually find in case reports from southern countries. In one of our cases we have also seen that treatment by light had a distinctly deleterious effect.

It is thus of importance to see that this disease also occurs in northern countries, and should be kept in mind. The result will be that even in cases of relatively benign looking tumours in the eyes, in conjunction with pigmented spots in the skin, the patients must be regularly controlled.

At a final examination of our patients, case 1 showed a new pterygium-like tumour of the same kind as the first one removed (see Fig. 8, Plate II), and case 2 showed pigmented spots and telangiectases in the conjunctiva. Both patients are therefore under control. In cases 1 and 2, familial investigations show that the disease is due to a recessive gene. Apart from local treatment eugenic measures must be taken to prevent the spread of this serious disease in the family. The members of the family should be instructed concerning the mechanism of heredity, and especially concerning the influence of consanguineous marriages.

### Summary and conclusion

The author reports the cases of a sister and brother and a case from another family with xeroderma pigmentosum and affections of the eye.

A brief account is given of x.p. and of melanomas in general and their treatment.

The difficulty of recognising x.p. at the initial stage is mentioned. In the first case the correct diagnosis was only established after years of observation. The ocular tumour in this patient, a recidivation after a removed pterygium-like condition, was thought to be a melano-malignoma and the skin-disease to be lentigenes.

During the years of observation, at the age of 17-27 years, constant re-appearing of malignant new-growths in different parts of the skin and metastasis to a gland were found. The malignancy of these were verified by microscopical examination. Further examination of the patient's family revealed the recessive nature of the condition, and made it clear that the fundamental disease was x.p.

The brother of the first patient has the same disease. The first malignant new-growth appeared here at the age of 27, and later he has had many of them at various places of the skin. This patient

also presented symptoms from his eyes. Naevi and telangiectases were seen in the conjunctiva.

The excellent result of X-ray or radium treatment in both of these cases is shown. The effect of both of them seems equally good. Mode and doses are specified.

Both patients are otherwise feeling well, and are still able to attend their usual work, and are now aged 27 and 32 years respectively.

The author further describes a third case of x.p. from another family. The affection of the eye appeared at the age of 10 years as a little whitish tumour of relatively benign appearance at the corneal limbus of the left eye. On renewed examination, at the age of 18, the tumour had infiltrated the whole cornea and parts of the sclera, and the eye was nearly blind. In the right eye there was a little whitish pinguecula-like tumour at the limbus. New-growths were found in the skin, and the malignancy was verified microscopically. Only then was the disease recognised as x.p. This patient was treated with silver nitrate and mercury oxide ointment. He also had a light-cure, which had a distinctly deleterious effect. Both eyes were blind at the age of 20 years, and were enucleated. The new-growths spread over the whole face, and the patient died when aged 21 years.

The result of the treatment in this case is compared with the results in the two first cases, and the question is raised whether a similar treatment with X-ray or radium might not have given a more favourable result. The clinical pictures were much alike in all three cases before treatment was started.

X.p. is rare in northern countries, the symptoms are vague in the beginning, and it probably takes a more protracted course here than in southern countries.

Special emphasis is laid on the fact that this disease must be kept in mind even in cases of seemingly benign tumours in the eyes when they appear in conjunction with pigmented spots in the skin.

Finally, mention is made of the eugenic measures that ought to be taken in order to prevent the spread of this serious, hereditary disease.

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## THE PRESENT STATE OF THE PROBLEM OF RETINITIS PIGMENTOSA\*†

BY

I. BIRO

BUDAPEST

AFTER the clinical characters of retinitis pigmentosa had been defined by the papers of van Trigt, Ruete, von Graefe, Donders and Leber, research turned towards the morphology and histology (Stock, Sukanuma, Ginsberg, Koyanagi, Schieck). Later research was directed toward the biological relations of the disease and the field of enquiry was considerably extended by the discovery of endocrinological factors. Investigations of possible connections between retinitis pigmentosa and the pituitary, thyroid, gonads and adrenals did not all lead to results of lasting value. But even the negative results were important, and the possibilities of endocrine involvement are now limited to the pituitary and the surrounding parts of the diencephalon.

During the latter half of the 30's when the part played by the pituitary and the hypothalamus became obvious, investigations turned to the question of inheritance.

The symptoms and groups of symptoms which so frequently are associated with pigmentary degeneration of the retina and originate within the pituitary and diencephalon suggest that these areas must play some part in the origin of the disease. The general metabolic disturbances, alterations of the water and salt metabolism, the low body temperature, the hypotony and cholesterinaemia (Lauber, Levy-Wolff) should be ascribed to factors within the diencephalon, and the inhibition of growth, adiposity, polyuria, syndactyly, genital hypoplasia, or polydactyly (Laurence-Moon-Biedl syndrome) are of pituitary origin. Deafness, dumbness, epilepsy, acrocyanosis, Raynaud's gangrene, are

\* From the Ophthalmological Clinic No. 1, University of Budapest.

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due to alterations of vasomotor innervation probably through the hormone of the posterior lobe of the pituitary (vasopressin) which plays a decisive part in eliciting them, and is a cause of the ever-present vaso-constriction seen in the fundus.

The appearance of pigmentation is not simply the consequence of an overgrowth of pigment at the site of the atrophy of the neuro-epithelium, but is also due to the effect of the melanophore hormone produced by the intermediate part of the pituitary which regulates pigment distribution.

It is thus evident that typical retinitis pigmentosa is, in the majority of cases, not an independent ophthalmic disease, but a manifestation of a widely branching complex, the nucleus of which is the pathologically altered functions of the pituitary and the diencephalon, and the hormonal consequences thereof. The cerebral symptoms associated with the fundus changes (which are in themselves a cerebral manifestation of the disease) correspond with the severity of these pathological disturbances of functions and secretions.

Is every case of retinitis pigmentosa an inherited one? The observations of Nettleship, Redslob, Franceschetti, Bucklers and the author among others, show that the answer is in the negative.

Nettleship as early as 1909 showed that retinitis pigmentosa could follow the acute exanthemata, loss of blood and injury to the blood vessels. Redslob at a meeting of the French Ophthalmological Society ("Ophthalmologica," 1947) showed a girl 14 months old who, a few days after a fever caused by vaccination, lost her eyesight. Her retinal vessels were spastic and her fundus anaemic. After some weeks the vision was gradually restored but the vessels remained narrow and the discs pale. The child was otherwise well, and the Wassermann reaction negative even in her more distant relations. Two years later an examination of the fundus showed typical retinitis pigmentosa.

A similar case was reported by Franceschetti, of a ten year old patient following vaccination. There was no vascular spasm but the discs grew pale, and after some years retinitis pigmentosa developed. Bucklers mentions its occurrence after rubéola and measles, Moreu after malaria, Sudarev after typhus. Redslob in a recent publication states that Lapersonne and Vassaux, as well as Kasas, found the histological signs of retinitis pigmentosa in the fundi of soldiers who had lost their sight from injuries.

The author's own observation concerns a woman of 60 years who in the summer of 1946 complained of a recent rapid loss of sight in the right eye. Vision was "fingers" at 20 inches. The fundus of the affected eye showed a marked degree of vascular

spasm, both arterial and venous. The disc and fundus were pale. No pigmentary changes were visible. There was no history of any acute illness. General medical and family history were negative, including Wassermann reaction. After an absence of two years she reappeared with the picture of retinitis pigmentosa in the right fundus, the left fundus being still normal. I believe that in this case the disease is to be attributed to some circulatory disturbance of unknown origin.

One-sided cases have been reported by other observers and in only a small fraction of them was it possible to trace a hereditary predisposition, and complications referable to pituitary or hypothalamus were rarely found. It may be concluded that accidental cases of retinitis pigmentosa following the exanthemata, typhus, malaria, wounds, inflammations, persistent vascular spasm and nutrition troubles, are not inherited, not of endogenous origin and not primarily of ectodermal character; and if the fundus picture is the same as that of the hereditary group it can only mean that the causation factors—toxins, etc.—specifically upset the secretory balance of the pituitary and thereby cause a hormonal dysfunction.

I therefore share Redslob's opinion that retinitis pigmentosa should be divided into two classes, the first being the hereditary, and the second the "sui generis" autonomous cases. The inherited affection, as shown clinically by the cerebral complication and histologically by the agreed findings, is primarily a neuro-cellular disease of certain areas of the brain and retinal elements which are structurally and ontogenetically related parts of the ectoderm.

The first group can be further sub-divided into the recessive and dominant types. The great majority are of recessive heredity, while those of dominant inheritance are of slighter degree and are generally free from complications (more than 300 own observations).

The autonomous type are not inherited, and are not systematically connected with the central nervous system.

The sub-division of retinitis pigmentosa into well defined groups ought to have beneficial effects on treatment, which has hitherto been handicapped by want of knowledge of aetiology.

The treatment of inherited forms of retinitis pigmentosa is hopeless, but that of the autonomous group is much more encouraging. The latest form of treatment, that of Filatov, should receive due attention. As far back as 1939 Filatov, in a joint paper with Verbickaja, published favourable results from intramuscular injections of suitably prepared cod liver oil. His

1945 publication deals with his cornea transplanting methods as well as with his new "tissue therapy." The essentials of this are that suitably prepared and controlled pieces of cornea, conjunctiva, liver, skin, cartilage, placenta, even vegetable matter like aloe leaf, are transplanted into the skin of the patient or beneath the conjunctiva, which substances, according to Filatov, act as "biogenic stimulators," which are not only effective against certain ocular diseases but stimulate also the normal functions of the eye. His method has been tried out on hundreds of patients with such varying disorders as corneal ulcers, trachoma, uveitis and retinitis pigmentosa. Of the last, 110 cases have been treated. No details of the results are available, but from reports reaching us through British and American periodicals (Gordon, Chentsov, Lipkina) interest in the matter is justified. Lacking information regarding the types of cases treated, the percentage of inherited and non-inherited—the forms of investigation with regard to aetiology, etc., it is difficult to express an opinion on the merits of a method, which cannot be denied originality.

The possibility of improvement, even lasting improvement in the autonomous cases cannot be excluded, but we cannot believe in any sort of biogenic stimulation which can alter an inherited pathological state of a part of the brain. This must be kept in mind by everybody who wishes to pursue a scientific attack on the problems of retinitis pigmentosa.

### Summary

Retinitis pigmentosa cannot be regarded as a uniform disease.

The author emphasises the dual pathogenesis of the disease as described by Redslob, namely: (1) inherited; (2) "sui generis" or "autonomous."

The inherited group is further divided into those of recessive and those of dominant inheritance.

In contradistinction to the hereditary form the autonomous is a sequel of the acute exanthemata, inflammations, toxic diseases, permanent circulatory impairment, etc., and the hereditary and autonomous—have certain clinical differences.

The latter does not exclude the possibility of permanent improvement, but no treatment can be expected to influence the inherited disease.

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## A CASE OF KERATOMALACIA CURED BY PENICILLIN AND VITAMIN A

BY

KAMEL RIZK

EL-MINIA, UPPER EGYPT

AS far as I know, the use of penicillin in the successful treatment of keratomalacia has not been recorded. For this reason I think that the detailed description of a case of keratomalacia treated very successfully with penicillin and vitamin A therapy is worth publishing.

### Case Report

On June 14, 1947, a male rural infant aged two years, was brought to my clinic with the following history:—towards the end of a short fever, of unknown cause, and of a duration of one week, both eyes started to become opaque, and the opacity increased rapidly. He was brought to my clinic three days after the onset of the opacity. On examination, he was found to be markedly emaciated and severely rickety, but he was not apathetic, the temperature was normal, and, apart from his eyes, there was no abnormality. Both eyes were kept open and blinked at long intervals. The conjunctiva of both eyes was dry with small whitish glistening spots on both sides of each cornea (xerotic spots). It was white without any signs of inflammation, and there was no discharge or lacrymation. Both corneae were markedly ectatic, dry, lustreless and ulcerated without any inflammatory reaction, either in the form of dilatation of the limbal vessels, or the growth of new vessels towards the ulcerated area. The right cornea was very opaque and infiltrated except for a narrow clear rim about 1 mm. in breadth at the periphery. The whole cornea was markedly ectatic, the centre of the cornea projecting forwards for a distance of about 4 mm. beyond its original site, so that the whole cornea became shaped like a cone with a flattened top. There was a transverse elliptical ulcer at the summit of the ectasia involving about one sixth of the whole corneal surface. The cornea at the site of the ulcer was not very thin except at one small spot. By applying a wisp of cotton wool to the cornea, most of its surface was found to be insensitive. The ulcerative process, *per se*, could not account for such a degree of ectasia of the whole cornea, and there must have been much softening and loss of elasticity of the whole corneal tissue to account for such a degree of ectasia occurring with normal intra-ocular pressure. Owing to the ectasia, the anterior chamber was deep, but there was no hypopyon.

The iris was dimly seen through the narrow clear periphery. The condition of the left cornea was generally similar to that of the right cornea, so that the above description applies to the left as well except that the clear rim at the periphery of the cornea was about 1.5 mm. in breadth, the ectasia was about 3 mm. and the ulcer was about one seventh of the whole corneal surface.

The absence of any inflammatory reaction, the softening of the corneal tissues as indicated by the severe keratectasia, the xerotic condition of the conjunctiva and cornea, and the bilateral occurrence of the affection as well as the general condition of the patient, all these signs made the diagnosis of the case as keratomalacia quite evident. Parsons (1934) said "A characteristic feature of keratomalacia is the absence of inflammatory reaction" and the absence of inflammatory reaction in this case leaves no doubt as to the correct diagnosis.

Keratomalacia is rare in Egypt. Its cause is primarily vitamin A deficiency, but complication by a microbial agent is sure to occur. Treatment should be directed against the microbial agent, for which penicillin must be tried, as well as against the vitamin A deficiency for which prepalin (Glaxo) injections are valuable. Penicillin therapy was started in the form of drops of a concentration of 2500 units per c.c. of distilled water. The mode of administration was that used by Sorsby (1946) in the treatment of ophthalmia neonatorum with slight modification. Two drops of penicillin solution were put in each eye every minute for half-an-hour, then every five minutes for another half-an-hour, then every half-an-hour. Apart from these penicillin drops and atropine ointment which was applied twice daily, no other local treatment was applied. No wash, no hot compresses and no protection by bandage were done. General treatment was not started. At 6 p.m., *i.e.*, seven hours after starting penicillin therapy, the periphery of each cornea became less opaque and the clear rim increased, slightly but definitely, in breadth. I was so impressed by the rapid improvement produced by penicillin that I was tempted not to start vitamin A therapy so as to be able to observe the sole action of penicillin. And I yielded to the temptation, fortunately without ill effect. In addition to penicillin drops which were used during the daytime and when the mother happened to be awake by night, one injection of 20,000 units of penicillin in oil and beeswax was given at 8 p.m.

Next morning the condition of each cornea was better, the opaque area growing less and the clear area increasing. Treatment consisted in half hourly drops of penicillin and 20,000 units in oil and beeswax at 8 p.m. Atropine ointment was twice applied. The same treatment was applied for the next two days.

On June 18, the area of the opaque tissue in each cornea was much

less than when first seen, but the growth of the epithelium over the ulcerated area was very slow, and no change was observed in the degree of ectasia. I decided to apply both local and general vitamin A therapy. Local vitamin therapy was applied in the form of a 20 per cent. haliver oil ointment with a eucerine base frequently, daily. General vitamin A therapy was applied in the form of intramuscular injections of 0.5 c.c. of prepalin (Glaxo) twice weekly (100,000 units per c.c.). After 24 hours of starting vitamin A therapy the epithelium covered all the surface. Penicillin therapy was stopped two days afterwards, and only vitamin A therapy, local and general, as well as atropine ointment twice daily, were continued.

On June 25, local dionine ointment 2 per cent. was applied once daily in addition to the above treatment. This 2 per cent. ointment was rapidly replaced by 5 per cent. and then 10 per cent. ointment once daily, and atropine was stopped.

In five weeks, *i.e.*, on July 19, there was a dense central leucoma in each eye, just covering the pupillary area, the rest of the cornea being clear, except for a few vessels growing towards the leucoma. All ectasia disappeared and the cornea resumed its original shape. Xerosis was cured. Optical iridectomy was not contemplated owing to the poor general condition of the patient, and it was thought best to consider it at a later date.

### Comment

This case is a severe one. Its severity is indicated by the above description as well as by the short history, probably correct, of three days. The prognosis in such cases is very bad. Basil Graves (1936) says that usually ulceration of keratomalacia is a bilateral rapid process, appearing in the centre of the cornea, leading to necrosis and rapid sloughing. He also says that the eye is not injected in this disease save when other complications occur (secondary infection). Penicillin, however, has revolutionized the prognosis in this case and acted dramatically. The response to penicillin in this case, when all inflammatory reaction was absent, indicated that some micro-organism which was penicillin sensitive, was present at a stage when the eye was not injected. This observation is contrary to the statement of Basil Graves mentioned above. However, the delayed growth of epithelium and the persistence of keratectasia, both responding to vitamin A therapy, point to the true aetiological factor in this disease, which is vitamin A deficiency.

It seems that penicillin should be given a trial in every case of keratomalacia, though its mode of administration need not be that described above. Certainly the method of subconjunctival injections, as described by Sorsby and Ungar (1947), is the best mode of penicillin administration in corneal affections. In keratomalacia,

subconjunctival injections of penicillin should be combined from the start with local and general vitamin A therapy, atropine ointment to the eye, as well as with any appropriate general treatment.

### Summary

A detailed description of a case of keratomalacia in an infant is given. Details of the treatment used and the progress made are mentioned.

A comment is made as to the proper treatment of keratomalacia with penicillin and vitamin A, with reference to the aetiological factors in this disease.

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## ON GENESIS AND OPERATION OF THE CICATRICIAL (TRACHOMATOUS) ENTROPION OF THE UPPER LID

BY

Prof. A. KETTESY

DEBRECEN

MOST operations for trachomatous entropion assume that the cause is the progressively incurved tarsus. Accordingly the solution has been sought in the straightening out of the tarsus, hence the operations of Celsus, Hotz, Nicati, Streatfeild, Snellen, Blaskovics, and their many modifications, generally with unsatisfactory results. Kuhnt's tarsectomy is an exception.

Observing closely the slow changes of the trachomatous entropion, it is not difficult to state, the turning of the tarsus appears late in the trachomatous process, preceded by a long and often stationary period, during which the intermarginal surface gradually merges with the conjunctival surface of the tarsus.

The entropion begins with the cicatricial shrinking of the tarsal conjunctiva, contracting into the well-known linear scar of the sulcus subtarsalis. The shrinking displays a traction in one direction upon the fornix, drawing it downwards, in the other direction upon the inner edge of the intermarginal surface. Thus arises the first stage of the cicatricial entropion: the rounding off of the posterior edge of the intermarginal surface. The line of the openings of the Meibomian ducts is directed against the eye.

The contraction continues and the intermarginal surface of the tarsus is rounded off into the conjunctival tarsal surface. In this second stage we see a sharp edge instead of the intermarginal surface; skin and conjunctiva are meeting in a line running just on to the surface of the eyeball.

As the contraction still progresses this line is also drawn inside. Only in this third stage is the eye coming in contact with skin. In very severe cases it happens that we see a fourth and last stage, when the tarsus itself has become crooked and deformed.

The trichiasis is only secondary: the effect of the drawing power, running along the surface of the lid reaches the line of the lashes,

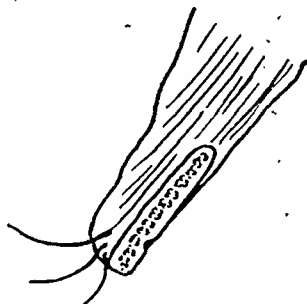


FIG. 1.

first the hindmost; in consequence of which the row of the cilia opens like a fan (Fig. 1).

We do not see always the above described regular progress, yet the same basic process and one of the stages may be always recognised.

From these changes the right solution can be deduced: the posterior half of the intermarginal surface has to be re-made, possibly of the same tissue and of course to last. There are proceedings that attain some more or less expressed posterior intermarginal surface as a by-result, while the aim has been to straighten out the tarsus or to raise the row of the eye-lashes.

Likewise, it is easy to understand, that all the operations called margino- or intermarginoplastics, cannot be of any use for trachomatous entropion. They all presume an intact tarsus and a normal posterior half of the intermarginal surface. Kuhnt's tarsectomy removes the support of the tarsal margin, therefore this is turning downwards, making a more or less expressed posterior intermarginal surface. Blaskovics' tarsoplasty (*inversio tarsi*) is the best example of the fact, that an operation devised on wrong conceptions may produce a good result.

Blaskovics intended to make an inverse curvature of the tarsus by turning it 180 degrees around its vertical axis. Of course this

could not lead to any result, but the execution of his idea made a tarsal incision necessary, bereaving the lower part of the tarsus of its support. As in Kuhnt's tarsectomy it produced a turning down of the marginal strip, uniting more or less rectangularly with the superior part of the tarsus.

We have had the opportunity of performing a long series of Blaskovics' tarsoplasty. From the comparison of the successful and unsatisfactory cases and from the interpretation of its manner

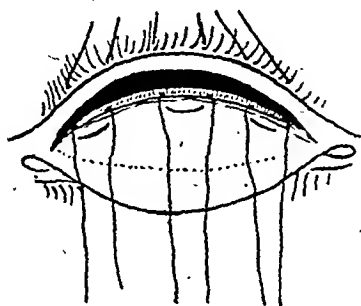


FIG. 2.

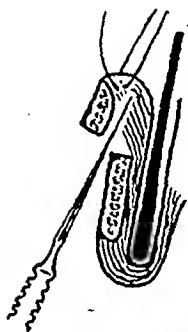


FIG. 3.

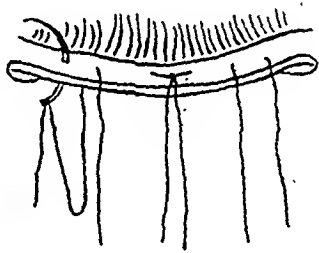


FIG. 4.

of acting, we have devised a new operation, the remodelling of the intermarginal surface out of the tarsus in a safe and simple way:

1. The upper lid is everted by Liebermann's sutures. Incision of the tarsus in the scar-line of the sulcus subtarsalis. The section has to penetrate through the tarsus perpendicularly and must divide it completely in its thickness and length.

2. Three mattress-sutures are inserted into the conjunctival margin of the section (Fig. 2). Every loop is about 4 mm. long. We take up also some tarsal tissue.

3. In order to facilitate the turning out of the marginal tarsal strip, we make an incision all along behind it, without buttonholing the skin (Fig. 3).

4. Lid-plate and Liebermann's sutures are removed, mattress sutures arranged, re-armed and brought through the marginal tarsal strip. The result depends chiefly on the correct position of these sutures. They have to go perpendicularly through the middle of the tarsal surface (Fig. 4).

5. After having them loosely knotted (in order to avoid cutting in during the next few days), the diverging ends are brought horizontally through the skin of the lid 10-12 mm. higher and knotted (Fig. 5). Thus we are preventing the tilting over of the new intermarginal surface and secure a thorough over-correction.

Vaseline dressing under slight pressure is made. Two days later the knots in the skin are removed. It would not be advisable to

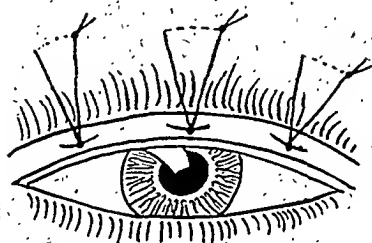


FIG. 5.

leave them any longer, they could cut into the lid-margin. The intermarginal sutures are removed on the sixth day.

Immediately after the operation we might consider that we had too much of an over-correction. We should never be afraid of it. The cicatricial contraction between the two tarsal pieces produces a rectangular position in any case; and 8-10 days later we see this result.

I have been performing this operation since 1930 for all stages and forms of trachomatous entropion with evenly satisfying result. It was published in *Ophthalmologica* in the year 1939, yet not exactly in the form now described, as the "turning out sutures," and some smaller modifications are newer additions. On the other hand the "folding sutures" proved to be superfluous. There I have presented photographs too; unfavourable changes in our life since that time have prevented further photographic recording.

In the above mentioned publication I have already pointed out that there are important differences between my proceeding and that of Panas, Sie-Boe-Lian, and Miric, who also make an incision in the sulcus subtarsalis and strive to attain rectangular apposition of the two tarsal pieces.

Lastly I would lay stress on the fact that I have had bad experience with all kinds of beads, rolls and any other pads laid below the knot in order to avoid cutting in of the sutures as it has

been so often recommended for the lid-margin. They all lead too easily to depressions or decubital ulcers, on the lid-margin which are particularly disfiguring. The exact but not tight simple knotting is the safest way, according to our experience.

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## CONTRIBUTION TO DATA ON SIGHT DISTURBANCES CAUSED BY PROLIFERATION OF PIGMENT EPITHELIUM\*†

(An unusual complication after cataract extraction)

BY

MAGDA RADNÓT

BUDAPEST

SIGHT disturbance of patients suffering from iridocyclitis and glaucoma may be caused by pigment deposits on the capsule of the lens.

In the case of iridocyclitis, especially when enlargement of the pupil is not performed in time, granulated pigment is found sometimes on the place of the synechia posterior. This is a remainder of the pigment epithelium. Correspondingly a lack of pigment may arise in the iris. After a time the pigment on the capsule of lens may gradually disappear.

It is well known that in the case of glaucoma the pigment of the iris may be scattered as this fact is mentioned as one of the causes for glaucoma. In such cases lots of pigment may be observed partly on the posterior surface of the cornea partly on the capsule of lens. In eyes treated for a long time with pilocarpine, pigment cysts are developed, pictures of them can be seen in Vogt's atlas. Pupils constantly contracted with pilocarpine, if they are allowed to enlarge, or are enlarged if possible with tonogen (adrenaline) show a surprising amount of pigment deposited on the capsule of the lens.

A remarkable and generally known change is that of the pigment epithelium of the iris and ciliary body in case of diabetes. The pupillary pigment layer is swollen and grey instead of being black as may sometimes be observed with a slit-lamp. This depigmentation is easily to be distinguished from injury or inflammation-caused depigmentation. This latter is usually discontinuous compared with the homogeneous depigmentation known in cases of diabetes. The aqueous humour of the anterior chamber flowing away at cataract

\* From the No. II Eye Clinic of the University of Budapest (Chief: Professor T. Nónay).

† Received for publication, February 9, 1948.



extraction may contain — as is well known — grains of pigment from the pigment epithelium. The same can be observed exceptionally with aged patients. Accumulation of glycogen and water in the pigment epithelium is the cause of the above described changes.

Serious disturbances of sight may be caused by proliferation of the pigment epithelium in case of after cataract and very seldom the structural change called "Pigmentnachstar" (Brückner) in German literature can be encountered. This is the case when the surface of the pupil is covered by a brownish-black layer. The layer is the cataracta secundaria which has a pigment deposit on its surface, but as histological examination revealed it is a result of proliferation of the iris pigment epithelium (Mans.).

A case essentially similar to the above description was observed without the presence of after cataract, proliferation of the pigment epithelium being found on the surface of the vitreous.

F.S. (:964-1947) woman aged 83 years had a cataract extraction on the left eye. Sight of the right eye was still perfect and therefore she used this eye. She did not get a glass for her left. She started to lose her sight 4 years ago and her sight is very bad this last year.

Status on entering the clinic: Right eye: perception: 5 m. localization: good. Left eye: counting fingers in  $1/2 + 10$  D.

Right eye: conjunctiva thin, pale. Lacrimal organs: no abnormality. Cornea smooth, shining. Chamber normal, aqueous humor clean. Pupil average large, good reaction. Iris without irritation. Lens homogeneously grey. No red reflex. Intra-ocular pressure 15 mm. Hg.

Left eye: conjunctiva thin, pale. Scar at the limbus after cataract extraction with iris attached to the cornea but not the pupillary edge so that the pupil is round with good reactions. At 12 o'clock basal coloboma in the iris. Iridodonsis. No after cataract can be observed even with enlarged pupils. Pupil and coloboma dark brown, with faint red reflex. Tension 15 mm. Hg.

Blood pressure 175/85 mm. Hg. Urine: alb., sugar, pus, negative. Hearing of patient is weak, medical diagnosis: arteriosclerosis.

Intra-capsular cataract extraction with complete iridectomy was performed being accompanied by slight bleeding from the vessels of the iris, which was not absorbed during the 10 days of clinical treatment. With atropine and poultice ordered, the patient was sent home. Ten weeks after the cataract extraction, sight of the right eye was 5/5. Vessels of retina sclerotic, otherwise normal. Left eye: as above described.

Examination of the left eye reveals immediately the brown colour of the pupil, which focally lighted seems to be a growth, its surface being convex, but even focally lighted or with scleral (Lange) lamp it is translucent, though keeping its brownish colour especially in the

inferior part of the pupil, it may be seen that there is only a thin brown layer.

Magnified by slit-lamp this seemingly simple brown layer is seen to cover the surface of the vitreous, and the homogeneous surface shows its moss like composition.

How far this pigmentation reaches behind the iris cannot be stated. It can be seen all over the surface of the vitreous when the pupil is maximally enlarged.

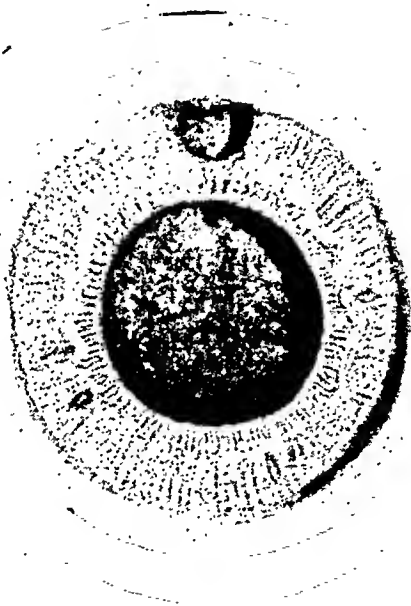


FIG. 1.

The question is how to explain this structural change.

It is obvious that a pigment layer covers the vitreous as it does in the case of a pigmented after cataract. In the case of the pigment secundaria the fact is easily understandable. Remnants of lens get easily into connection with posterior layers of the iris. In case of cataract extraction complicated by inflammation, the iris may be attached to the vitreous. Thus we have to assume in our case that the iris epithelium got into contact with the vitreous layer the epithelium injured somehow started to proliferate and covered the anterior surface of the vitreous. The assumption is that some disturbance of healing had occurred as in our case anterior attachments are to be seen to the nasal part of the basal coloboma, (*See Figure*). The pigment epithelium of the iris seems to have been injured while cutting or at the reposition of the iris.

## Summary

An unusual complication was observed which developed after cataract extraction.

After intra-capsular cataract extraction with a round pupil in a woman of 83 years, the surface of the vitreous was covered by a pigment layer, similar to pigmented after cataract (so called Pigment-nachstar) causing her serious sight disturbances.

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## A CASE OF PYOCYANEUS RING ABSCESS OF THE CORNEA TREATED WITH STREPTOMYCIN \*

BY

J. MASCHLER

HAIFA

RING abscess of the cornea is a rare and always a dramatic event for the oculist. Its treatment until a few years ago was a most ungrateful task. Since the appearance of the sulpha drugs and the modern antibiotics new hopes have arisen. The number of cases published since then is so small, however, that I may be justified in reporting a favourable effect of streptomycin treatment on a ring-ulcer caused by *Pseudomonas aeruginosa* (*B. pyocyaneus*).

### Case History

The 15 years old apprentice M. St. was hurt on August 15, 1947, by a tiny splinter of iron which stuck in the superficial layers of his right cornea near its centre. It did not hurt him very much, and he appeared in the eye-infirmary of the worker's Sick Fund only two days later. There was already a small infiltration around the foreign body which was easily extracted. He received atropine, hot poultices were ordered, and when he came back the next day, there was no change for the worse. I, myself, saw the patient only on the third day of treatment, when he told me that during the previous night he had felt unbearable pains in the hurt eye which had become blind during the last few hours. The eyeball was highly irritated, the whole right cornea, save a narrow peripheral rim of 1 mm., was occupied by a large abscess, the central part of which was slightly

\* Received for publication, December 3, 1947.

transparent. A hypopyon filled a quarter of the anterior chamber. The green-blue hue of the pus immediately raised the suspicion of a pyocyaneus infection, and it was confirmed on the next day by culture. As I had no streptomycin at my disposal I provisionally used penicillin. 100,000 units of pure white penicillin were dissolved in 2 c.c. distilled water, half of it was injected under the conjunctiva, the anterior chamber was punctured, the hypopyon removed, and two drops of the solution introduced into the anterior chamber. The remaining content of the vial was injected intramuscularly, and in addition 500 units of vitamin C into the cubital vein. The patient was admitted to hospital, hot cataplasms, atropine, and 6 grms. of sulfadiazine daily were prescribed. The father of the young patient with much difficulty succeeded in getting hold of 5 ampoules of streptomycin within two hours, and from then on it was applied every 3 hours intramuscularly, instilled into the eye hourly, and injected under the conjunctiva daily. On the second day of his stay in hospital 2 drops of the streptomycin solution (2,500 units) were introduced into the anterior chamber. This procedure was much more painful than introducing penicillin, but no doubt it was more useful. The patient received totally 1 gm. streptomycin daily, and in addition repeatedly powdered boric acid and sulphathiazole into the conjunctival sac, and sulfadiazine per os 6 grms. daily.

After the beginning of this intensive treatment, the purulent corneal infiltration did not proceed further, though the anterior chamber kept on filling with thick pus. On the third day of streptomycin treatment only, when a broad Saemisch's section was performed, the corneal infiltration rapidly declined. Two days later marked regression of the whole inflammatory process was established. The cornea became more lustrous and transparent, and the clear peripheral zone, chiefly in its upper part, broadened to 2 mm. The top margin of the atropine widened pupil became visible; the patient was able to distinguish hand movements before the eye, and light projection was correct; tension -1. The patient remained in hospital for two more weeks. When dismissed he still had slight ciliary irritation, the cornea appeared somewhat flattened and to a large extent occupied by a leucoma, through whose more translucent centre the pupil was distinctly visible; the cornea regained its normal lustre, and on the nasal side there was a peripheral anterior synechia. Tension was at first -1, but a few days later secondary glaucoma appeared which ultimately compelled me to antedate the already contemplated iridectomy. It was performed *ab externo* on October 16, 1947. After an uneventful post-operative course, the tension dropped to normal. Vision for the moment is finger-counting only, in spite of a broad coloboma; though its further improvement may be expected.

## Comment

It seems clear that the quick control of the fulminating infection was brought about by the intensive streptomycin therapy. Five grms. of it were applied systemically in the course of 5 days, apart from the initial dose of 100,000 units of pure white penicillin, and 36 grms. sulfadiazine during 6 days. In addition streptomycin was given twice subconjunctivally and once into the anterior chamber.

In order to make sure that streptomycin was the effective factor, the strain of pyocyaneus was tested in the bacteriological laboratory of Dr. W. Hirsch for its sensitiveness to streptomycin. It became evident that 500 units were able to check the growth of the bacteria, whereas 50 units still allowed it.

The publications about therapeutic effects in pyocyaneus infections in the era of sulpha-drugs, penicillin and streptomycin are rather sparse and it appears that we have still not got over the stage of tentative trials. The effect of even high doses of sulphathiazole against pyocyaneus meningitis was not encouraging<sup>1</sup>. The same applies to penicillin which finally was summed up as inefficient against pyocyaneus in most handbooks. The case of Alpert<sup>2</sup>, however, shows that it is not always true. He succeeded in stopping a ring abscess of the cornea caused by pyocyaneus and staphylococcus aureus haemolyticus with intracameral injection of only 75 units of penicillin, though in combination with sulfadiazine and typhoid vaccine within a week. Owens<sup>3</sup> reports in August, 1946, a ring abscess of the cornea caused by *Escherichia coli* which he was able to stop by hourly instillation of streptomycin.

Adcock and Plumb<sup>4</sup>, and Pool and Cook<sup>5</sup> report in two very instructive papers on the influence of streptomycin on infections of the urinary tract caused by a mixed flora of *aerobacter aerogenes*, *B. coli* and *B. pyocyaneus*. They pointed out that although in all their cases fever and pyuria promptly subsided, only the *aerobacter* group quickly disappeared in the urine, whereas *B. coli* and *B. pyocyaneus* were found a long time afterwards. They conclude that both *B. coli* and *B. pyocyaneus* respond to streptomycin on a limited scale only.

Just because of the many discrepancies contained in the reports mentioned above, I have felt obliged to add my case to the small number so far recorded.

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OPERATIVE TREATMENT OF FIVE  
CASES OF IRIDODIALYSIS\*

BY

SÜREYYA GÖRDÜREN

ANKARA

TRAUMATIC iridodialysis is not uncommon. It disturbs the patient because of the cosmetic and functional defects, such as dazzling, decreased visual acuity, and unilateral diplopia. Hence early treatment is necessary.

Although operative treatment was first performed by Amedée (1866), and later by some other ophthalmologists, it did not attract attention and general interest till Golowin (1917).

Iridodialysis may be single and so small as to be hardly seen by the naked eye, or large and multiple. The minute dialysis is often covered by an arcus senilis or the upper lid, and is not visible. Those that are new and without any disfigurement in the pupil may be left and no operative treatment is necessary.

Cases of total dialysis do not require surgical treatment so long as they do not develop secondary glaucoma.

In the operative treatment of iridodialysis many procedures are put forward. They may be divided into two general groups:

1 — Operations which are based upon the incarceration of iris root between the lips of a keratome incision or impinging the iris root against the posterior surface of the cornea by means of 2 or 3 sutures (van Lint, Key, Jameson).

2 — Those which are based upon grasping and pulling the iris root between the lips of a keratome incision with an iris hook or forceps, and performing the operation without any suture (Golowin).

The following five cases have been treated with some modification of the Golowin operation.

After local anaesthesia a keratome incision is made just on the level of the iris root and parallel to its anterior surface. The knife is slowly withdrawn and the iris root allowed to come between the lips of the incision with the outflow of aqueous humour; then with two spatulae slight adjustments are made to keep the iris root evenly in the lips of the wound. Atropine solution of 1 per cent. is instilled, and both eyes are covered. Next day there was no dialysis. There was a slight groove in the pupil of the first case (Fig. 2), while in the second there was no difference between the operated and normal eyes (Fig. 4).

The day after operation we allowed the patients to sit up in bed, with their back reclining on the pillow, the third day allowed them

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\* Received for publication, October 15, 1947.

to walk in the room, and the seventh day opened the eye and let them resume their work.

In the third, fourth and fifth cases the dialyses were larger and very old (3-12 years). The iris root which we tried to insert between the lips of the wound by means of a spatula easily escaped. We therefore inserted the iris hook between the iris and the lens and caught it in the central part of dialysis just close to the iris root; brought it between the lips and, moving the hook laterally, let the hook free. Then using the spatula, the lateral parts of the iris root were stroked between the lips of the wound; atropine was instilled, and both eyes were closed.

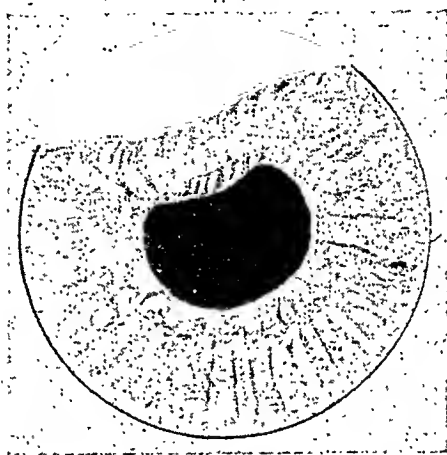


FIG. 1.



FIG. 2.

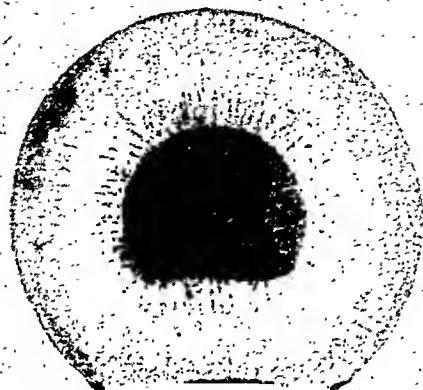


FIG. 3.

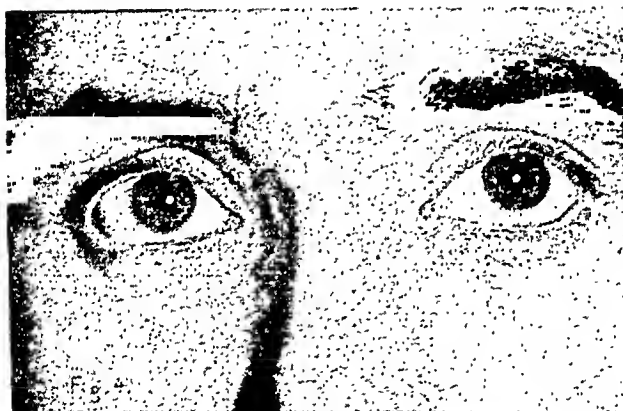


FIG. 4.

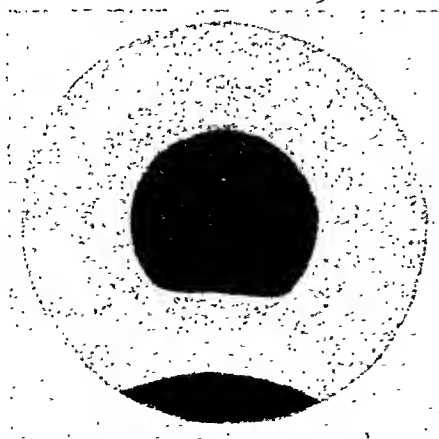


FIG. 5.



In cases where the first procedure is not possible, the second procedure consisting of pulling the iris root with an instrument, is applied. There is the danger of damaging the lens. For this reason I prefer to catch the iris from behind with the tip of the

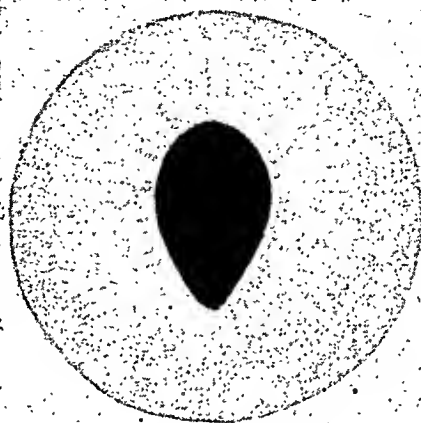


FIG. 6

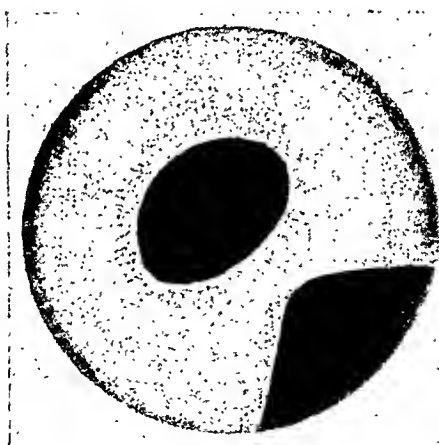


FIG. 7.

hook upwards. To use iris forceps seems more dangerous for the lens.

Although iridodialysis was corrected in the last three cases, it left a deep groove in the pupil margin (Figs. 6, 8, 10).

We believe that the first method is preferable to the others. Here

there is no danger of damaging so fine a tissue as the iris by grasping it with iris forceps or hook. This method is also safe for the lens.

In this method the iris root having been incarcerated evenly and in a smaller extent the pupil has a more regular shape compared

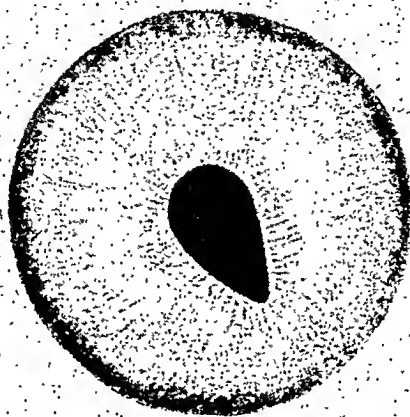


FIG. 8.

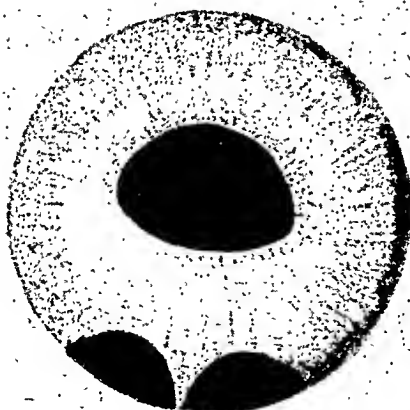


FIG. 9.

with the cases where a sharp groove is caused by traction with forceps or hook.

Wheeler (1934) recommends avoiding an operation on iridodialysis, unless there is a good reason for it, and even then adopting a simple method.

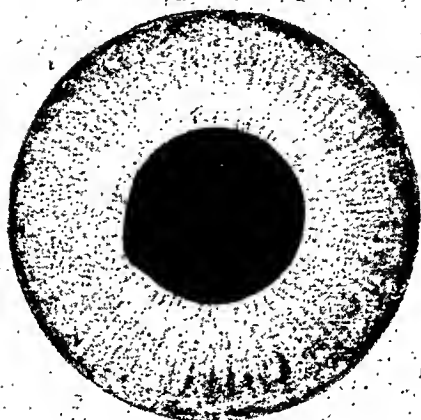


FIG. 10.

Encouraged by the simplicity of the operative procedure, and by good cosmetic and functional results, we believe that the operative treatment of iridodialysis is necessary.

### Case reports

(1) O.S., a young man aged 21 years, complained of dazzling and poor vision of the left eye. Three months ago a stone struck his left eye.

There was an iridodialysis in the left eye about at 11 o'clock meridian (Fig. 1). There were traumatic lens opacities, and partly atrophic pigmented patches in macular region. He could count fingers at  $1\frac{1}{2}$  metres distance. After operation dialysis was corrected (Fig. 2), he could count fingers at 1.5 M., and there was no dazzling.

(2) S.U., a young man, aged 22 years, complained of monocular diplopia and a poor vision in the left eye. Three months ago a stone had struck his left eye. There was an iridodialysis at 6 o'clock meridian (Fig. 3). There were traumatic lens opacities and pigmented patches in the macular region. He could count fingers at  $1\frac{1}{2}$  metres distance. After operation iridodialysis was corrected (Fig. 4), vision 10/200, and no diplopia.

(3) H.K., a young man, aged 22 years, complained of dazzling in the right eye. Ten years ago a piece of iron had struck his right eye. There was an iridodialysis at 6 o'clock meridian (Fig. 5), vision 20/25. After operation dialysis was corrected (Fig. 6), vision 20/20, and no dazzling.

(4) S. D., a young man, aged 22 years, complained of dazzling

in the left eye. Three years ago the butt of his fowling-piece hit him on his left eye.

There was an iridodialysis at 4.30 o'clock meridian (Fig. 7), vision 20/25. After operation dialysis was corrected (Fig. 8), vision 20/20, and no dazzling.

(5) M. K., a young man, aged 20 years, complained of dazzling and poor vision in the right eye. Twelve years ago a piece of stone had struck his right eye. There were two iridodialyses, separated from one another by a narrow bridge, one at 5.30 and the other at 6.30 o'clock meridian (Fig. 9). There were traumatic lens opacities, vision 20/100. Three operations were performed. Now no dialysis (Fig. 10), and no dazzling. Visual acuity same as before.

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## SIX CASES OF SCINTILLATIO ALBESCENS\*

BY

SÜREYYA GÖRDÜREN

ANKARA

SCINTILLATIO albescens is one of the endogenous deposits in the vitreous. The latter, as a whole, is not frequent. Dor found 32 cases in 82,732 patients, and Westphahl 40 cases in 65,000.

They were known even in pre-ophthalmoscopic days, but until Benson (1894), little was known about the types of the disease. He divided them into two groups:

1. Asteroid hyalitis.
2. Synchronis scintillans.

The former type occurs in normal vitreous, and consists of white, spherical bodies; while the latter occurs in a fluid vitreous and appears as sparkling gold particles.

The cases to be described are typical examples of the first group.

1. R. G., a man, aged 58 years, complaining of weakness and weariness, was admitted to Gülhane Hospital. He was suffering from a mild diabetes for 16 years, and was leading his normal life with a mild diet.

His last blood serum examination revealed, when hungry, 248 mg. per cent. of glucose, this rose to 325 mg. when given 50 g. of glucose,

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and to 356 mg. after a second dose of 50 g. Arterial blood pressure 70/145 mm., red and white B.C. count, blood picture, and internal organs were normal. Mantoux test and Wassermann reaction were negative, sedimentation rate 5 mm.; blood serum nitrogen within normal limits, cholesterol 208 mg. per cent., no abnormality in liver function.

The eye examinations showed a cuneiform cataract in both eyes, vision being 20/20. The ophthalmoscopic examination made after the pupil had been dilated revealed the presence of small, disc-shaped or spherical white opacities, waving with the movements of the eye. They were too small to be seen by transmitted light.

Slit-lamp examination showed the presence of highly dispersive opacities. They had a golden gleam and looked larger than the

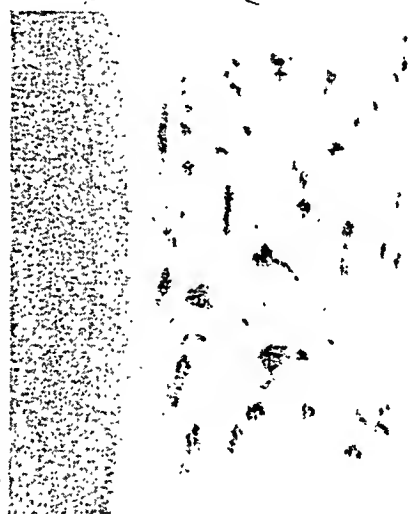


FIG. 1.

real size; while examination of each opacity by direct focal illumination revealed the fact that they had a dead white colour (Fig. 1).

They were discrete or marshalled in strands or had peculiar figures resembling an acacia leaf or a bunch of grapes, which moved with the movements of the eye, but returned to their original place without settling to the bottom of the vitreous chamber.

The vitreous of the left eye had a normal appearance.

2. F. O., a man, aged 65 years, was first examined on July 15, 1946. He complained that his left eye had poor vision. He had an incipient cortico-nuclear cataract, and a refractive error of  $-4.0$  D. in both eyes. The left fundus revealed superficial retinal haemorrhages and yellowish white patches just above the macular region.

The fovea had a pale yellowish colour and there were small pigment dots around it. As to the visual acuity after correction, the patient could count the extended fingers at one metre with his left eye; while that of right eye was 20/50.

On careful examination, after the pupil had been dilated, the presence of fine pigmentary disturbances were also seen in the right macular region (senile macular degeneration of Haab).

During ophthalmoscopic examination, gleaming spots were observed in the vitreous of the right eye. Slit-lamp examinations confirmed the presence of asteroid bodies. Here, unlike the first case, the anterior part of the vitreous was practically free from the asteroid bodies.

The patient had no systemic disorder. Urine analysis showed nothing pathological. Arterial blood pressure 90/150 mm.; X-ray examination of the chest revealed nothing pathological. Mantoux test and Wassermann reaction were negative, and sedimentation rate 4 mm. Blood serum sugar within normal limits, nitrogen 28 mg. per cent. and cholesterin 230 mg. per cent.; no abnormality in liver function.

3. A. D., a woman, aged 51 years, was seen on November 18, 1946.

There was incipient senile cataract in both eyes, and several posterior synechiae and a secondary glaucoma in the right. Visual acuity, R. 10/200, L. 20/60.

There were asteroid bodies in the left vitreous.

Urine analysis showed nothing pathological. Arterial blood pressure 85/160, and internal organs were normal. Mantoux test and Wassermann reaction were negative. Four infected teeth were removed. Blood serum nitrogen 22 mg. per cent., sugar 85 mg. per cent., and cholesterin 225 mg. per cent. Liver function test revealed nothing pathological.

4. Z. O., a man, aged 52 years, seen on February 5, 1947. There was immature senile cataract and a refractive error of - 1.0 D. in both eyes. Vision after correction, R. 20/30, L. 20/200.

There were typical asteroid bodies in the right vitreous.

Wassermann reaction and Mantoux test were negative, sedimentation rate 3 mm., internal organs normal, arterial blood pressure 110/210. No focal sepsis. Microscopic examination of urine sediment revealed several erythrocytes. Blood serum nitrogen 37 mg. per cent., sugar 128 mg. per cent., cholesterin 150 mg. per cent. Liver function test showed no abnormality.

5. Z. O., a woman, aged 63 years, seen on February 19, 1947. There was an incipient senile cataract in both eyes, multiple haemorrhagic patches in the left fundus, and a circinate retinopathy, secondary optic atrophy and typical asteroid bodies in the right eye. Vision, R. perception of light, L. after correction, 20/50.

Wassermann reaction negative, Mantoux test slightly positive, sedimentation rate 40 mm., R. and W. B.C. count and blood picture normal. Blood serum sugar 107 mg. per cent., nitrogen 27 mg. per cent., cholesterin 195 mg. per cent. There was a slight albuminuria. Liver function test showed no abnormality.

6. S. B., a woman, aged 50 years, seen on May 20, 1947. There was no ocular abnormality but a slight degree of hyperopia. Visual acuity after correction 20/20 in both eyes.

Internal organs were normal. Arterial blood pressure 120/220, Wassermann reaction negative, Mantoux test slightly positive, sedimentation rate 25 mm. There was alveolar pyorrhoea, and slight albuminuria.

Blood-serum sugar normal, nitrogen 40 mg. per cent., cholesterin 202 mg. per cent. Liver function test revealed nothing pathological.

Benson named this disease asteroid hyalitis. But the term of "hyalitis" is inappropriate, hence asteroid bodies is a better one. Argyll Robertson described this condition as "snowball opacities" and Wiegmann called it "scintillatio albescens or nivea."

According to the existing literature the disease is not common. Rutherford (1933) collected the records of 56 cases from the literature.

During a period of less than a year, we have seen six cases out of 14,350 eye patients. So it seems to be more frequent than is generally recognised. It is frequently overlooked, since it does not give any subjective symptom.

We have noticed that even the least visible cases can easily be detected by observation of several gleaming points in the ophthalmoscopic field. But usually they are confused with the light reflecting from the anterior face of the lens and cornea. Hence they do not attract attention.

Scintillatio albescens is a disease of old age. The age of incidence, as seen in the literature, varies from 30 to 84, the average being 60. Our cases varied between 50 and 65. According to the records in the literature the disease is three times as common in males as in females. In our cases both sexes are equally affected. All of our cases are unilateral, 5 out of 6 being in the right eye.

Some authors had the opportunity to examine chemically and histologically the asteroid bodies; all agree that they are composed chiefly of calcium soaps.

An association with some general disease (arteriosclerosis, nephritis, diabetes, syphilis, tuberculosis) or local disease (choroiditis, cyclitis, retinal haemorrhages or thrombosis) has been claimed. But in some cases no general or local disease can be discovered.

In the six cases under consideration, we found an association with

diabetes in one case, with hypertension in 3 cases and with focal infection in one case. No general or focal disturbances could be found in any.

As to local disturbances, in one case there was no disturbance except a slight hyperopia. in 5 cases there were cataracts of incipient or immature stages. This was associated with senile macular degeneration in one, and circinate retinopathy in the other.

In the majority of cases, the cholesterol content of the blood, although within normal limits, was somewhat increased.

Possibly some changes in the composition of the blood may cause the deposition; and local disturbances may act as a precipitating factor. Thus association with some general disturbance or focal infection, structural changes of the lens, circinate retinopathy, or senile macular degeneration may be the cause of deposits. But since the lens changes and macular degenerations are bilateral, the monocular incidence of scintillatio albescens needs some further explanation.

We applied treatment according to the general or local disturbances, but could not see any improvement in the fundus picture.

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## CONGENITAL CYCLOPIA AND ORBITAL CYST TOGETHER WITH OTHER DEVELOPMENTAL ANOMALIES ON THE SAME SIDE OF THE FACE

BY

F. PAPOLCZY

BUDAPEST

ACCORDING to Seefelder there are four groups of developmental anomalies of the whole eyeball:

- (1) Mikrophthalmus congenitus;
- (2) Anophthalmos congenitus;
- (3) Mikrophthalmos seu anophthalmos congenitus et cysta orbitae;
- (4) Cyclopia.

Congenital anophthalmos is mostly a developmental anomaly of both sides, more rarely of one side only, according to literature.

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\* Communication of the Municipal St. Stephen Hospital of Budapest, Ophthalmological Department (Chief physician: F. Papolczy, M.D.). Received for publication, April 12, 1948.



The rudiments of the eyeball, however, can nearly always be found by clinical or by microscopic examination of the soft parts of the orbit. For this reason it is impossible to distinguish exactly extreme degrees of congenital microphthalmos from anophthalmos. This anomaly is nearly always to be seen together with an orbital cyst. The cyst is sometimes so large that it causes the eyelid to bulge, in other cases so small that it can only be detected by microscopic examination. It mostly forms under the lower lid.

Congenital anophthalmos is a hereditary developmental anomaly. It was sometimes found to be a consequence of intermarriage. In other cases secondary injuries to the embryonal development of the eyeball must be taken into consideration, which may be any sort of injury, even such as caused by experimental research work.

Microscopic examination of the orbital cyst shows that this is of ectodermal origin. It develops in the primary optic vesicle or in the already developed optic cup. When the cyst has developed in the primary optic vesicle, there are but one or more coherent cavities to be found which are filled with a mucous secretion rich in albumen. They are lined with a tissue which resembles the retina or the pigment epithelium, sometimes similar to glia. If the cyst originates from the already developed optic cup it generally grows very large, and the microphthalmos or rudiment of the eyeball may be found in the orbit.

On February 14, 1947, a boy infant of ten days was sent from the children's ward of the St. Stephen Hospital to the ophthalmological department for examination.

Ophthalmological report: on the right side, above the inner canthus, starting from the inner third of the upper lid, a thick, proboscis-like structure, 3.5 cm. long and 1-1.2 cm. wide hangs down parallel to the nose into the sulcus nasolabialis, its lower end showing a navel-like, deep depression. The lower lid is violet-blue, greatly enlarged, hemispherically protruding and like an air-cushion to the touch. It is almost impossible to open the palpebral fissure. There is no eyeball. In its place a conjunctival sac pressed upwards from below is visible. Besides, the baby has a hare-lip and cleft palate. The left side is normal.

Röntgen picture: The right orbit is narrower, in it an increase of shadow about the breadth of a finger from above-outside downwards towards the middle which entirely fills out the orbit in the profile picture.

Operations: On February 17, the proboscis-like structure was removed, on May 17, we excised the cyst which was situated under the lower eyelid. It was almost as large as a nut and filled with a mucous, pale yellow fluid. Both operation wounds healed perfectly.

Histological report: a section of the proboscis-like structure under the microscope presents a picture resembling the tissue of the nose. The outer wall of the section is formed by several layers of stratified epithelium under which tissue numerous fat- and sweat-glands are to be seen. In the centre there is a round small lumen the walls of which consist of epithelium resembling that of the outer wall. Between the two layers of epithelium loose tissue, in some places filled with blood vessels, is present, the lumen is almost entirely surrounded by thin, ring-shaped cartilaginous-tissue.

The wall of the cyst is surrounded by tissue fibres and lined with two, in some places more layers of epithelium, partly presenting a polypus like structure.

On May 24, seven days after the second operation, the baby became feverish; the highest temperature was 39.1 C. The otologist diagnosed otitis media purulenta of the left ear. Two



Congenital cyclopia and orbital cyst.

days later pneumonia set in. In spite of penicillin and other treatment usual in such cases, the baby died on the eighth day of the illness.

Report of the post-mortem examination of the soft parts of the orbit: in the section retina, choroid, ciliary body, iris and particles of the lens are visible in a normal disposition, in many places pigment epithelium is present.

Thus, in my case, the baby had congenital anophthalmos and an orbital cyst on the right side, and, on the same side a proboscis, that is to say a rudimentary nose, further a hare-lip and cleft palate. Under the microscope rudiments of the eyeball were visible in the soft parts of the orbit.

Actually the developmental anomaly I describe here belongs to the "cyclopia"-group, the changes in the eye and nose generally being only a part of the injury to the forebrain.

According to Bock there are the following degrees of cyclopia:

(1) Two separate orbits, situated near to each other, and a rudimentary nose (cebocephalia).

(2) Two separate orbits, so near to each other that the proboscis-like nose is above them (arhinencephalia).

(3) Two separate eyes in a common orbit.

(4) The same, but the sclera of both eyes glued together.

(5) Common, but thinner sclera in which are two eyes and the optic nerves close to each other.

(6) One cornea, the other tissues of the eye twofold and the optic nerves attached to each other.

(7) Two lenses in one eye.

(8) One eye.

This grouping, however, is by no means complete, because many other kinds of anomalies of the development of the eye may occur, from the different forms of coloboma to microphthalmos and anophthalmos.

Freaks born with cyclopia are mostly unable to live.

Besides anomalies of the eye the place of the second proboscis-like nose may vary to a great degree. Very often all sorts of other developmental anomalies of the other parts of the face may be seen simultaneously. Consequently it is evident that it is most difficult to classify the different forms of cyclopia and that on account of the many variations of developmental anomalies not two cases are exactly identical.

Lately Meeker and Aebli described a case that was already published in 1942 and 1944, and that has a resemblance to mine. A boy of  $5\frac{1}{2}$  years had two eyes in a common sclera on the left side, a proboscis (rudimentary second nose) on the same side, and hare-lip and cleft palate as well.

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## ANNOTATION

## "What's in a Name?"

The question is one which has often been asked, and in medicine one might be tempted to reply—"a good deal more than was ever meant to be in it, and sometimes the exact opposite." The classical example is the word "artery" derived from the Greek *ἀέρηνειν*, meaning to hold air, and so called because the tubes the words designate were thought to carry air from the heart or trachea, as Trevisa wrote in 1398 "to bere and brynge kindly heete from the herte to all the membres." Any attempt to change artery to a word meaning "carry blood" would, however, rouse strenuous opposition, and could only result in a much less elegant one.

Several examples are to be found in our own branch of medicine, the best known being cataract and glaucoma. "Cataract" has been attributed by some to the ancient theory that it was caused by a fall of inspissated material into the pupil, but others derive it from the second meaning which was "portcullis." This is more rational, because as the portcullis obstructs vision in a gateway, so does the cataract obstruct vision in the eye.

Glaucoma is a useful word, because being meaningless—literally translated, it signifies a gray-green tumour—it serves to cover our uncertainty as to the pathology of the disease.

Hypermetropia and myopia might come in for criticism, since the former means an eye beyond measure—a curious phrase to apply to an eyeball whose usual defect is that it is too small and the latter a closed, and therefore by inference a small eye, but it is doubtful whether micropia and megalopia would ever be accepted as respectively synonymous, even though they described the condition more accurately.

That a knowledge of Classics is not always a help to medical students was demonstrated in an examination held a few years ago at a certain hospital. One of the questions consisted in asking the meaning of various ophthalmological terms, among which were epiphora and hyperphoria. Epiphora was correctly defined by a candidate as an overflow of tears, but hyperphoria was beyond him, so he summoned his knowledge of Greek to his aid, and stated that hyperphoria meant a really good cry.

## BOOK NOTICES

### **Clinical Ophthalmology (for general practitioners and students).**

By H. M. TRAQUAIR. 264 pages, 72 illustrations (including 8 coloured plates). Henry Kimpton, London, 1948. Price 25/-.

A book which purports to discuss "Ophthalmology without an ophthalmoscope" must come as something of a shock to us. It certainly takes us back a hundred years; and the chapter on "Impairment of the Sight without Obvious External Signs" wherein such conditions as choroiditis, vascular spasm, retinal haemorrhage, retinal detachment and optic atrophy are differentiated by indirect evidence from subjective symptoms such as the onset and completeness of visual failure and such objective signs as the pupillary reactions, makes the reader dream he is re-reading Sir William Mackenzie. The plea is made that the book is written for the student and the general medical practitioner who is not experienced with the use of apparatus; but are the students of Edinburgh University not taught that the ophthalmoscope is one of the essential aids to the complete physician, and has the general practitioner totally forgotten the teachings and admonitions of Osler? In many cases it may unfortunately be so; but is it wise to encourage them in their evil-doing? To do so requires courage: and invites criticism.

Within this very severe limitation the book is a very lively and interesting one. After an elementary description of the anatomy, physiology and external examination of the eye and two brief chapters on the causation and general therapeutics of ocular affections, the diseases of the visual apparatus and its adnexa are discussed seriatim. Chapters are also devoted to functional ocular manifestations, the eye in infancy, childhood and old age, and the final chapter on popular (and medical) misconceptions and prejudices is a mine of common sense—spectacles do not weaken the eyes, near work does not hurt them nor does light; reading in bed is a harmless pleasure, close work at school does not make the myopic more myopic, and so on. A study of the book will be of great value and some entertainment (for it is well written) to the general practitioner and will be able to answer many questions and solve many difficulties in his daily work thereafter; but we wish the author had not led the reader to suppose that the ophthalmoscope, with all its value not only in diagnosing ocular complaints but in general medicine, were an instrument that he could neglect with a clear conscience.

### **The Oculorotatory Muscles.** By RICHARD G. SCOREE (St. Louis).

359 pages, 113 figs. Henry Kimpton (London). Price 40/-.

This book presents a general review of the entire subject of the anatomy, physiology and functional pathology of the extra-ocular

muscles. The first section (of 6 chapters) deals with the anatomy and physiology of the muscles, their innervation and mechanics and the physiology of binocular factors. The second section (of 7 chapters) discusses latent deviations in the position of rest, modern views on the concept of orthophoria and the symptoms and treatment of heterophoria. The third section (of 3 chapters) deals with manifest deviations in a general way—the aetiology of squint followed by a detailed discussion of the comitant and non-comitant varieties. The fourth section (of 6 chapters) is concerned more minutely than is generally the case with diagnostic procedures. The subject is gone into in considerable detail—the case history and its significance, visual acuity, the measurement of the deviation, the angle kappa, ductions, versions, vergences, diplopia fields, abnormal correspondence, the significance of head and face tilting, false orientation and so on. The last section (3 chapters) deals shortly and only on general lines with treatment, non-surgical and surgical. The author quotes extensively from recent literature, accepting the work of Bender and Weinstein on the intimate topography of the oculomotor muscles, and drawing largely from the writings of Bielschowsky, Duke-Elder, Lancaster, Adler, Cridland, and—particularly—Chavasse. The difficult question of the diagnosis of the muscle at fault in parietic squints is gone into in the orthodox way but with all the refreshing enthusiasm of the writer of a good detective story—the search for clues, the deductions therefrom, and the satisfaction of the sleuth in unravelling a mystery are all there. In the section on treatment, non-operative methods are dealt with cursorily in six pages. On surgical treatment the author deplures the present tendency towards the adoption of rule-of-thumb methods—the lengthening and shortening of a muscle by a specified and pre-determined number of millimetres, or the empirical procedure, for example, of employing a recession-and-resection operation on the lateral recti in innumerable non-analysed cases of lateral heterotropia. Each case, the author insists, must be considered on its own merits and surgical treatment should be individualistic depending on an adequate appreciation of the pathology and diagnosis. In general, he holds Chavasse's view that it is better to "weaken" the antagonist of a parietic muscle than to advance or resect the weaker muscle: such an operation is, in this view, a "strengthening" one in that the formerly parietic muscle is allowed more freedom of action and scope to regain much of its function.

The book is well produced and interestingly written; it forms a useful compilation of modern views on a difficult and intriguing subject.

**The Anatomy of the Eye and Orbit.** By E. WOLFF. 3rd Edition. 440 pages. 322 figs. (21 coloured). London, H. K. Lewis, 1948. Price 45/-.

It is pleasant to welcome the third edition of this excellent descriptive anatomy of the eye, the ocular adnexa and central nervous connections. The book is becoming the standard work on this subject, and the new edition deserves to maintain the position won by its predecessors. The most important addition is in illustrations, more than eighty of which have been added, and when it is noted that the majority of these have been prepared from the author's own specimens, no one will be surprised that they are of unusual excellence. The book has been brought up to date and includes much new material on the pupillary pathways, the external geniculate body, the ciliary muscle, the cornea, the vitreous and zonule, the retinal capillaries and a number of other subjects. The abundance of the illustrations, the clarity of the text, the maintenance of interest by the frequent reference to practical clinical points which have an important anatomical bearing all combine to make the book outstanding. The author and his publisher are to be congratulated.

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## NOTES

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### NATIONAL HEALTH SERVICE

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#### Supplementary Ophthalmic Services: Notice to Ophthalmologists

It is understood that the Ophthalmic Services Committee of each Executive Council will be required to publish a list of medical practitioners and opticians, having the prescribed qualifications, who undertake to test sight on the terms obtaining in the Committee's area. The expression "medical practitioner having the prescribed qualifications" means a medical practitioner who has:—

- "(a) completed an academic or post-graduate course in ophthalmology approved by the Committee hereinafter in this paragraph mentioned, and received a diploma or certificate in respect of this course; or
- (b) held for a period of two years an appointment as an ophthalmic surgeon or assistant ophthalmic surgeon on the staff of an eye hospital or a hospital having a special eye department; or

(c) held any appointment for a period of two years affording special opportunities for acquiring the necessary skill and experience of the kind required for the services to be rendered ; or

(d) had, immediately before the appointed day his name included in the list of medical practitioners prepared by either the B.M.A., The National Ophthalmic Treatment Board or the Incorporated Ophthalmic Council, for use by Approved Societies for the purpose of Ophthalmic Benefit under the National Health Insurance Act, 1936 ;

and who shall, to the satisfaction of the Minister, acting on the advice of a Committee to be recognised by him for the purpose of approving such qualifications, have had adequate *including recent* experience."

The Central Professional Committee referred to above has been appointed by the Minister and is composed of practitioners nominated by the B.M.A. and the Faculty of Ophthalmologists. This Committee has the duty of compiling a central list of medical practitioners having the prescribed qualifications. The Committee therefore invites applications from all ophthalmic medical practitioners to be included in the central list, which is an essential preliminary to inclusion in local lists for which separate application must be made to the Ophthalmic Services Committees of the Executive Councils concerned.

Inclusion in the central list is entirely without prejudice to future action and it will be open to every practitioner to decide, when he knows the terms of service, whether he will take part in the Supplementary Ophthalmic Service or not. Ophthalmic practitioners should not, however, await the publication of the terms of service before applying for recognition by the Central Committee.

All ophthalmic practitioners are therefore requested to apply as soon as possible to the Secretary, Ophthalmic Qualifications Committee, B.M.A. House, Tavistock Square, W.C.1, giving the necessary evidence that they comply with the criteria outlined above. It is particularly important that details of recent experience should be included.

### Supplementary Ophthalmic Services : Notice to Ophthalmologists in Scotland

A separate central list of medical practitioners having the prescribed qualifications for participation in the Supplementary Ophthalmic Service will be compiled for Scotland. Application forms received at B.M.A. House, London, from practitioners in Scotland will therefore be automatically forwarded to the Scottish Secretary, B.M.A. House, Drumsheugh Gardens, Edinburgh, for submission to the Scottish Qualifications Committee.



Oxford  
Ophthalmological  
Congress  
July 8, 9, 10.  
Programme, 1948

THE Congress opens with an address of welcome by the Master, Mr. F. A. Williamson-Noble; after which a discussion will take place on "The Use and Abuse of Topical Ocular Therapy," to be opened by Mr. F. Ridley, Dr.

F. E. Preston and Dr. J. M. Robson. Papers occupy the time till 4.30, when tea will be taken in the gardens of Balliol College. The annual dinner is at 7.15 p.m.

The second day opens with a commercial exhibition: Papers follow until 11.15 a.m., when Sir Stewart Duke-Elder gives the Doyne Memorial Lecture.

In the afternoon a discussion on "the operative treatment of chronic glaucoma" will be opened by the Master and by Mr. Maurice Whiting.

The last day is given over to papers.

\* \* \* \*

British Medical  
Association.  
Section of  
Ophthalmology.  
116th Annual Meeting,  
Cambridge, 1948

JULY 1, 1948, Morning Session, Thursday, 10 a.m. Opening Papers: (1) Mr. Juler—

"Ophthalmic Problems associated with Gynaecological and Obstetrical conditions." Followed by Mr. Nutt. Afternoon, July 1, 1948, 2.30 p.m.

Occasional Papers: A. G. Cross—"The present day position of contact lenses." J. D. Currie—"Optical Aids to the other man's job." P. H. Beattie—"Heredity of Eye Diseases." H. Ryan—"Nutritional Eye Diseases."

July 2, 1948, Morning Session, Friday, 10 a.m. (2) Mr. Recordon—"The Significance and Interpretation of Refraction." Followed by Mr. A. Lister, Mr. V. Purvis. Afternoon, July 2, 1948. Clinical meeting at Addenbrooke's Hospital at 2.30 p.m. 3.30 p.m. Films:—"Detachment," "Intra and Extra Capsular Cataract Extraction," "Strabismus and Glaucoma," by Mr. H. B. Stallard.

Officers of the Section.—*President*: O. Gayer-Morgan; *Vice-Presidents*: E. G. Recordon; O. M. Duthie, J. H. Doggart; *Hon. Secretaries*: G. F. Wright, A. G. Cross.

\* \* \* \*

The University  
Eye Clinic of Munich

We understand from Professor Weve of Utrecht that Professor Wesseley, who was expelled by the Nazis before the 2nd World War, has re-started the University Clinic at Munich. His age is 75 years.

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Corrigendum

On page 129, 2nd line, the reference to our Volume for 1945 should have been XXIX not XXX as printed.

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

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No. 8

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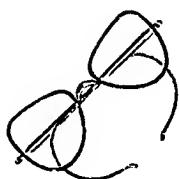
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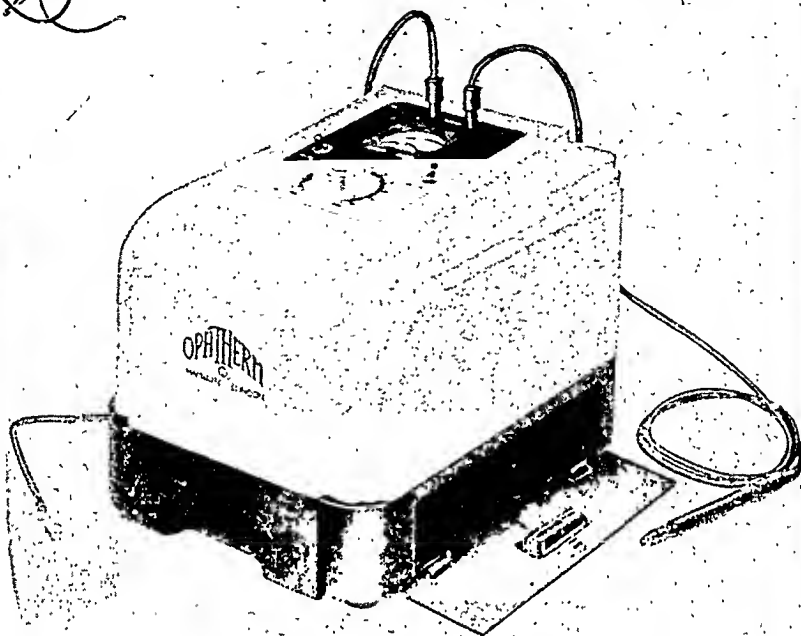
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## OPHTHALMIC DIATHERMY

(THE OPHTHERM)



The apparatus illustrated above has been designed and specially developed for retinal detachment operations.

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# THE BRITISH JOURNAL OF OPHTHALMOLOGY

AUGUST, 1948.

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## COMMUNICATIONS

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### INTRAVITREOUS STREPTOMYCIN: ITS TOXICITY AND DIFFUSION\*

BY

P. A. GARDINER, I. C. MICHAELSON,

R. J. W. REES *and* J. M. ROBSON

FROM THE DEPARTMENTS OF PHARMACOLOGY AND PATHOLOGY, GUY'S  
HOSPITAL MEDICAL SCHOOL, AND THE TENNENT INSTITUTE  
OF OPHTHALMOLOGY, UNIVERSITY OF GLASGOW

THE discovery of the new antibiotic, streptomycin, by Waksman and his colleagues in 1944, has put at our disposal a substance capable of producing a chemotherapeutic action on organisms not particularly susceptible to other agents. Gram negative organisms and *M. tuberculosis* are the organisms for which streptomycin is particularly effective. Previous work has shown that streptomycin does not easily penetrate through the cornea (Leopold and Nichols, 1946) and it was decided to investigate the concentrations of the

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\*Received for publication, June 25, 1948.

drug attained in ocular fluids following its administration (1) into the vitreous and (2) subconjunctivally. It is known that drugs injected into the vitreous may produce damage, sometimes severe, to the retina (Duguid *et al.*, 1947) and an investigation of the action of streptomycin on the eye tissues following its intravitreal administration was therefore also undertaken. The results of Bellows and Farmer (1947) published in the meantime would suggest that streptomycin is non-toxic to the retina and can safely be administered by the intravitreal route.

### Methods

Two samples of streptomycin were used in these experiments and we are greatly indebted to the Antibiotics Study Section of the U.S. Public Health Service (through Dr. Seger) for supplying these. The pure sample was used for the intravitreal toxicity tests; it was streptomycin hydrochloride calcium chloride double salt (Pfizer lot X 76), and its biological activity against *B. subtilis* was 719 u/mg. For the diffusion experiments the second sample of commercial streptomycin (Merck) was used.

For the diffusion experiments 2,000  $\mu$ g. of streptomycin was injected into the vitreous in 0.1 ml. of sterile saline by the method previously described (Duguid *et al.*, 1947). For the toxicity experiments two doses were used, *viz.*, 1.2 mg., and 3.0 mg., injected in 0.1 ml. saline. In these latter experiments the eyes were observed at regular intervals for periods of 12 to 112 days and the changes noted. The eyes were then removed and examined histologically.

The method for assaying streptomycin in the aqueous and vitreous was based on the measurement of the diffusion of streptomycin through agar. The melted nutrient agar (Stebbins and Robinson, 1945) was seeded with a 24 hour culture of the Mayo Clinic strain of staph. aureus to a final dilution of 1/1000 and added to a series of glass tubes. After the tubes had cooled for five minutes small quantities of the eye fluids for assay were added above the agar. Four tubes were used for each eye fluid. The tubes were incubated at 37° C. for 24 hours and the zone of inhibition between agar-eye fluid and line of growth was measured in millimetres. The measurements were made by fixing a tube on to a slide, placing it on the mechanical stage of a microscope, and viewing the zone of inhibition through a 2/3 inch objective with a pointer attached. The transverse millimetre scale gave readings to the nearest 0.1 mm. With suitable controls of 2 and 64  $\mu$ g. per ml. a graph was constructed from which the unknown fluids were estimated.

It was shown that streptomycin control solutions made up in saline gave identical zones of inhibition to those made up in buffered aqueous or vitreous and so the former were used for convenience throughout. The method is much more reliable if the fluids for assay are kept alkaline. All ocular fluids were therefore diluted with an equal quantity of m/10 phosphate buffer at pH 7.8 before assaying.

The method is accurate to within  $\pm 20$  per cent. and gives a reading down to  $0.5 \mu\text{g.}$  per ml. Even small quantities of  $0.2 \text{ ml.}$  of aqueous are sufficient for four estimations by this method.

The concentration of streptomycin in aqueous and vitreous was measured, by the above method, 24, 48 and 72 hours after the injection of  $2,000 \mu\text{g.}$  streptomycin in  $0.1 \text{ ml.}$  sterile saline into the vitreous (see Table I).

TABLE I  
Concentration of streptomycin after intravitreal injection of  $2,000 \mu\text{g}$  streptomycin.

Time after injection, hours	Rabbit Number	Concentration of streptomycin ( $\mu\text{g. ml.}$ )	
		Aqueous	Vitreous
24	36* R. Eye	41	—
	L. Eye	$<0.5$	—
	37* R. Eye	84	—
	L. Eye	$<0.5$	—
	38 R. Eye	43	340
	39 R. Eye	46	200
	40 R. Eye	86	215
48	41 R. Eye	20	—
	42 R. Eye	34	—
	43 R. Eye	24	—
72	44 R. Eye	12	—
	45 R. Eye	13	—

\* Right eye only received streptomycin injection.

In another smaller series the concentration of streptomycin in the aqueous was measured 3, 6 and 24 hours after subconjunctival injection of  $10,000 \mu\text{g.}$  streptomycin made up to a total volume of  $0.2 \text{ ml.}$  in  $1/1000$  adrenalin (see Table II).

TABLE II

Concentration of streptomycin after injection of 10,000  $\mu\text{g.}$   
in 1/1,000 adrenalin subconjunctivally.

Time after injection, hours	Rabbit Number	Concentration of streptomycin ( $\mu\text{g. per ml.}$ ) in aqueous
3	1	20
	2	8
6	3	0.8
	4	0.5
24	5	<0.5
	6	<0.5

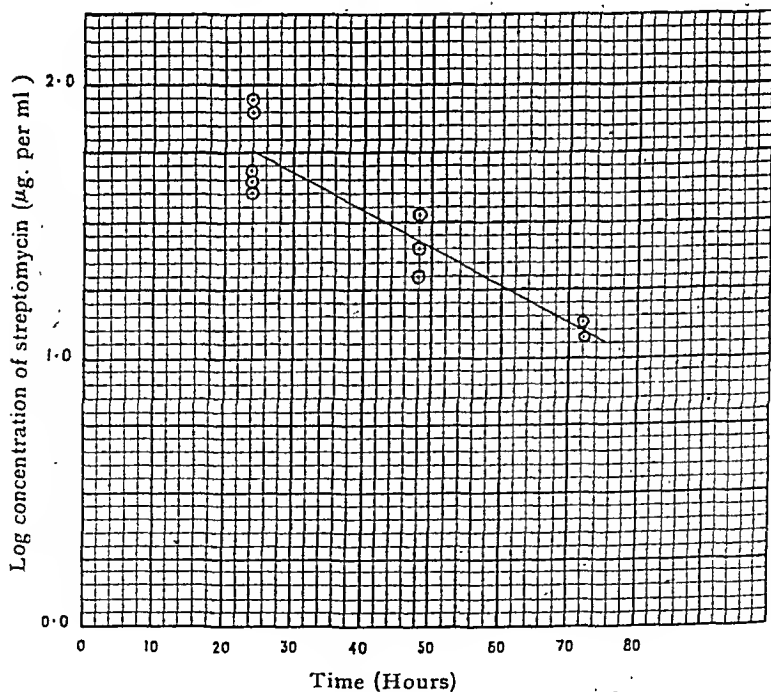


FIG. 1.

Concentration of streptomycin in aqueous after intravitreal injection of 2,000  $\mu\text{g.}$  of streptomycin. Aqueous-vitreous ratio at 24 hours = 0.25.

For the toxicity experiments streptomycin was injected into the vitreous of the right eyes of five animals while as a control 0.1 ml. of normal saline was injected into the vitreous of the left eye in each case. One animal received seventeen doses of streptomycin subconjunctivally over a period of 20 days, when the globe was examined histologically.

## Results

### 1. Diffusion of streptomycin.

The results are given in Tables I and II and shown graphically in Figs. 1 and 2. It will be seen that after the intravitreal injection of 2,000  $\mu$ g. of streptomycin, this acts as a depot and chemotherapeutic concentrations are maintained in the ocular fluids for over three days. The diffusion of streptomycin is therefore appreciably slower than that of penicillin, the data for which (previously described by Duguid *et al.*, 1947) are also shown in Fig. 1, A.

On the other hand the subconjunctival injection of a larger dose

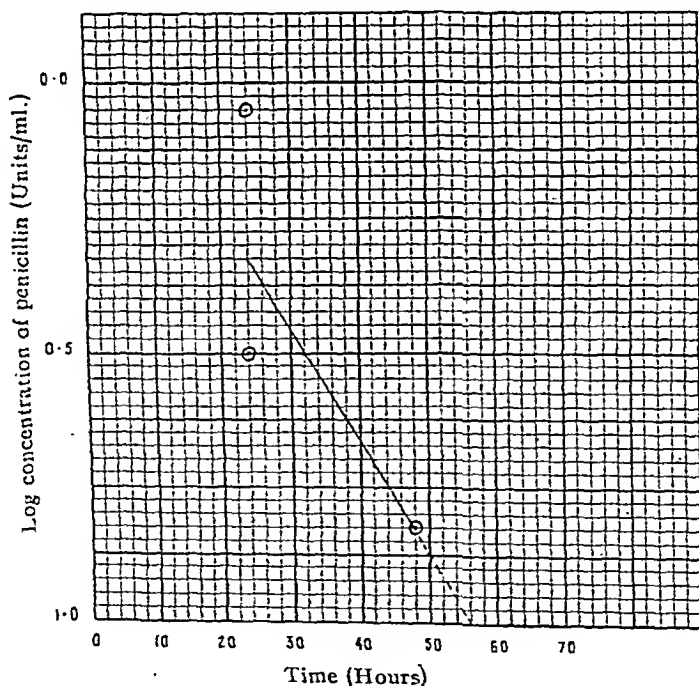


FIG. 1A.

Concentration of penicillin in aqueous after intravitreal injection of 2,000 units of penicillin. Aqueous-vitreous ratio at 24 hours = 0.01.



of the drug (10,000  $\mu\text{g.}$ ) combined with adrenalin to delay the rate of absorption produced a chemotherapeutic concentration in the aqueous for only a short period (Fig. 2).

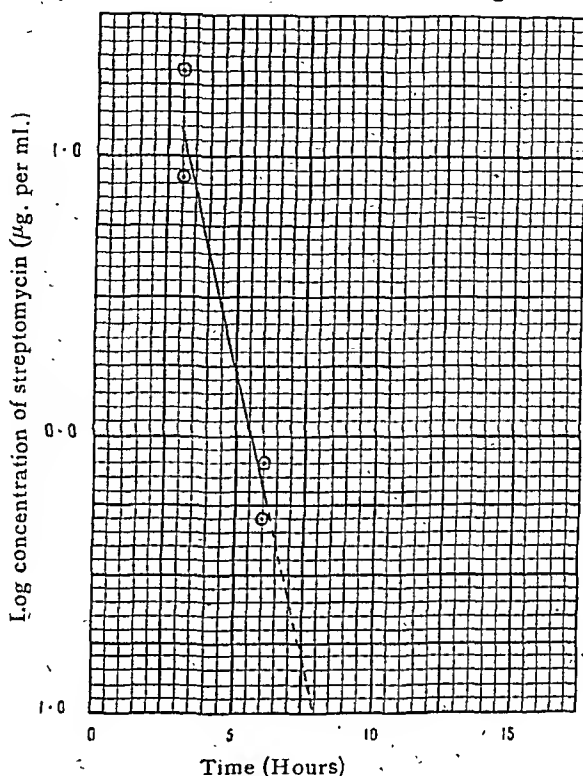


FIG. 2.

Concentration of streptomycin in aqueous after subconjunctival injection of 10,000  $\mu\text{g.}$  of streptomycin in 1/1000 adrenaline.

## 2. Toxicity of streptomycin.

Five animals were injected with streptomycin. Two of them (128 and 129) received 1.2 mg. in 0.1 ml. saline into the right eye and 0.1 ml. saline into the left (control) eye. The periods of observation were 77 and 112 days. The other three (130, 131 and 132) received 3.0 mg. in 0.1 ml. saline into the right eye and 0.1 ml. saline into the left eye. The periods of observation were 12, 77 and 112 days.

The retinal changes following the intravitreal injection of streptomycin were pronounced.

The two eyes which received 1.2 mg. showed only trifling and transitory immediate oedema but pigment stippling was extensive after one week in one and after two weeks in the other. Both

showed patchy retinal atrophy in the region of the disc and medullated fibres, about a week after the pigment stippling appeared. The globes after fixation were bisected in front of the ora serrata and the lesions noted clinically identified with the help of the slit-lamp. The affected portions of the fundus were excised, embedded in paraffin and the sections stained with haemalum and eosin. In one fundus there can be noted a gross loss of the cellular elements of the retina over a large area with migration of pigment into it from the hexagon pigment layer. In the other eye there is over a large area a disturbance and loss of the outer retinal elements. In neither case does the choroid appear to be affected. The larger dose (3.0 mg.) produced even more distinctive changes. In one (131) the whole inferior retina became atrophic after a period of oedema followed by pigment changes. The other two animals (130 and 132) showed deep oedema immediately after the injection and shortly afterwards widespread pigment reticulation began to be noticeable. Histological examination of the three eyes receiving the larger-dose shows in all of them extensive loss of all retinal elements over large areas with massive pigment infiltration of the retina. In one eye the retina was almost completely detached.

In the retina of the eye which received subconjunctival injections of streptomycin no changes were found, either clinically or histologically.

One control eye showed some exudate in the central third of the inferior periphery of the retina. The vitreous of the other eye had been injected with 3.0 mg. streptomycin.

#### Summary of the toxicity experiments

It is clear that streptomycin has a deleterious effect on the retina when it is introduced into the vitreous in doses of 1.2 or 3.0 mg. It would not appear to have any toxic effect on the fundus when given subconjunctivally.

#### Discussion

After a single intravitreal injection of 2,000  $\mu$ g. of streptomycin an effective therapeutic concentration was maintained in the ocular fluids for at least three days. This slow rate of diffusion of streptomycin is similar to that obtained by Bellows *et alii* (1947) using 25 to 100  $\mu$ g. of streptomycin per injection. From this point of view a single intravitreal injection of streptomycin might well be sufficient to deal with certain ocular infections in man.

On the other hand the present findings show clearly that even

1.2 mg. (863  $\mu$ g. of activity) of pure streptomycin produces serious and permanent retinal damage. These observations are at variance with those of Bellows *et alii* (1947), who showed that intravitreal streptomycin in amounts of 25 to 1000  $\mu$ g. per injection failed to give rise to any permanent damage to the fundus. Their series of experiments was done using solutions of various commercial lots and a purified sample of streptomycin and were also followed by ophthalmoscopic and histological examinations. Our toxicity series was done on a pure sample of streptomycin (Pfizer X 76) and we have seen similar changes with the ophthalmoscope in eyes injected with commercial streptomycin. The difference between these findings may well be due to differences in the toxicity of the streptomycin used, but the data suggest that at present great caution should be used in the intravitreal use of streptomycin.

### Summary

(1) Intravitreal injection of 2,000  $\mu$ g. of streptomycin acts as a depôt from which streptomycin diffuses away slowly, chemotherapeutic concentrations still being present in the ocular fluids after three days.

(2) The toxic effects of streptomycin introduced into the vitreous in dosages of 1.2 and 3.0 mg. result in marked retinal damage.

We are grateful to the W. H. Ross Foundation (Scotland) for the Prevention of Blindness who have defrayed part of the expenses of this work.

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AN ANALYSIS OF FIBRE-SIZE IN THE  
HUMAN OPTIC NERVE\*

BY

L. W. CHACKO

DEPARTMENT OF HUMAN ANATOMY,  
UNIVERSITY OF OXFORD

DATA on the fibre-size "spectrum" in the optic pathways must form an essential anatomical preliminary to electro-physiological studies of the visual neural system. Extensive studies on peripheral nerves have brought to light some of the factors on which the differences of calibre of nerve fibres appear to be based. Studies of fibre-size in the central nervous system have been carried out by Häggquist (1936) on the spinal cord, and by Szentágothai-Schimerl (1941) on several of the important pathways of the brain.

It has been recognised from the time of Gudden (1886) that the optic nerve contains myelinated fibres of graded size. Arey and his co-workers in their extensive investigation on the quantitative (and to a certain extent qualitative) composition of the optic nerve in a series of vertebrates, observed that in man all the fibres are myelinated and are of widely varying size. A considerable body of electro-physiological work on the optic nerve has been completed on frogs, rabbits and cats, and attempts have been made to group the fibres in this nerve on a physiological basis using conduction rate, threshold to electric stimuli, refractory period, time to maximum, etc., as criteria for grouping. In the histological study which this work entailed the authors arbitrarily distinguished certain fibre-sizes and attributed to them certain physiological properties. As yet, however, no systematic analysis of the range and frequency of the fibre-sizes in the optic nerve has been attempted. The importance of this investigation is emphasised by the findings of Granit that the electrical activity in the optic nerve (as recorded from its constituent fibres by his micro-electrode technique) indicates a specific sensitivity of the related receptors and their associated neurons in the retina to monochromatic lights. Such elements in the retina, possessing specific sensitivity to different wave-lengths of light, will give rise to impulses which are probably conducted along nerve fibres of one particular type in preference to others. The qualitative variations of nerve fibres so far recognised are the varying thickness of the axis cylinder and of the myelin sheath, and the presence or absence of the sheath of Schwann and the nodes of Ranvier. The present investigation deals with fibre-sizes, which are analysed in detail.

**Material and methods**

Human optic nerve sections of  $5\mu$  thickness were prepared and several standard silver and myelin stain techniques were employed.

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\* Received for publication, May 7, 1948.

Of these, Weigert-Pal preparations were found most suitable for measurement, while the others were used for the purpose of checking and confirmation. The particular specimen which was used for measurement was the optic nerve of a man, aged 61, in whom no defective vision or any other affection of the visual system was reported. No reduction in the size of the fibres of the central nervous system is apparent at that age according to the report of Szentágothai-Schimert (1941).

In order to measure the diameter of the fibres and to group them simultaneously, a method was devised (Allison and Chacko, 1948) in which an Abbé camera lucida was used to superimpose the image of a scale with lines of graded thickness corresponding to the range of size of the nerve fibres in the optic nerve. The scale is so prepared and calibrated that when the width of a line coincides in its image with the diameter of a nerve fibre it indicates the actual diameter as well as the size-group to which it belongs. Thus, it is possible to arrange the fibres into groups of smaller range than those adopted by Häggquist or Szentágothai-Schimert. A square corresponding to  $(60\mu)^2$  area of the microscopic field and containing 25 small squares each  $(12\mu)^2$  was drawn and fixed under the mirror of the camera lucida. The nerve fibres in each small square were measured one after the other and ticked off. From the average number of fibres within the area  $(60\mu)^2$  the total number of fibres in the optic nerve was also estimated in the usual way.

It was found that in a well-prepared section the myelin rings are undistorted and in fibres cut transversely appear as smooth circles. However, in their course through the optic nerve, the constituent fibres undergo a certain amount of rearrangement and in cross-sections of the nerve, many fasciculi may be seen running a more or less oblique course as they change their relative positions. Such fibres appear in sections as oval or rod-shaped, and in this case it was decided to take the short diameter as approximating to the true diameter of the fibres. The total diameter of the fibres (including the myelin sheath) was measured in each case. Measurements of about 4,000 fibres contained in fifteen fields of  $(60\mu)^2$  along eight radii of the cross-sectional outline of the nerve were taken and grouped in  $\frac{1}{2}\mu$  ranges. The frequency percentages of these groups were then calculated and a histogram was drawn.

### Results

The human optic nerve contains fine, closely packed, myelinated fibres without Schwann sheaths; these fibres exhibit a continuity in range of size from the smallest to the largest diameter (Fig. 1). The minimum calibre measured was  $0.7\mu$  and the maximum  $8.0\mu$ , and very occasionally fibres of  $10.0\mu$  sizes were also noted (Fig. 1c). The histogram (Fig. 2) shows that the greatest frequency of the fibres is under  $1.0\mu$  and the next greatest from  $1.0$  to  $2.0\mu$ , at which

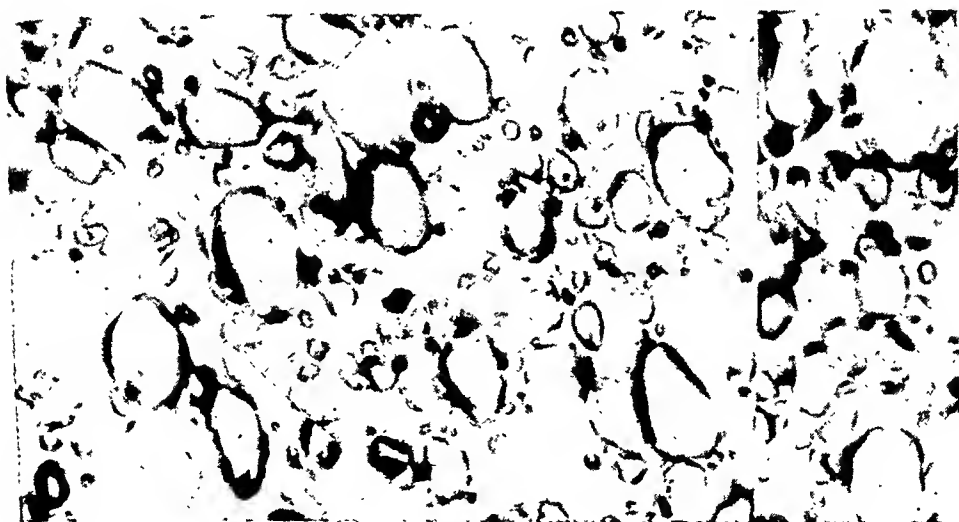
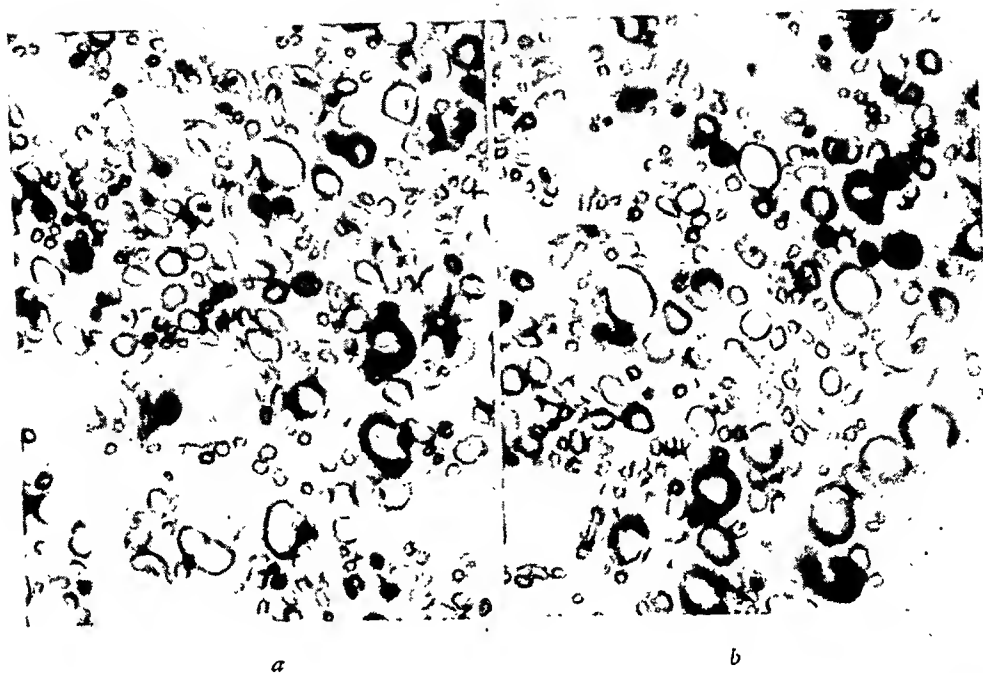


FIG. 1.

Microphotographs of Weigert-Pal preparations of the optic nerve in man. Magnification  $\times 1000$ . (a) Note the variation in the sizes of fibres, their distribution, and the predominance of small fibres of about  $1\mu$  size. (b) In this particular region fibres of  $4-6\mu$  size appear in greater number. (c) Microphotograph of the same preparation from regions where large fibres of about  $10\mu$  form the outstanding feature.



level the frequency drops rather steeply towards the base line and then more gradually in the direction of the larger fibres with an indication of a second low rise in the region of  $5.0$  to  $7.0\mu$ . This last feature was more pronounced in confirmatory measurements carried out from other preparations.

Minute "dots and rods," mentioned by Brodal and Harrison (1948) as indicative of the possible existence of minute myelinated fibres in the central nervous system, were not particularly evident in any of our preparations although their presence could not be positively excluded. Moreover, the continuous range that characterises the sizes between  $0.7\mu$  and  $8.0\mu$  did not extend below  $0.7$  down to the sizes indicated by "dots and rods" that may be present. The total number of optic fibres in the human optic nerve was estimated to be between 815,000 and 1,000,000 fibres.

### Comments

The histogram of the fibre-calibre of the optic nerve corresponds very roughly to the first of the two peaks of the fibre size histogram

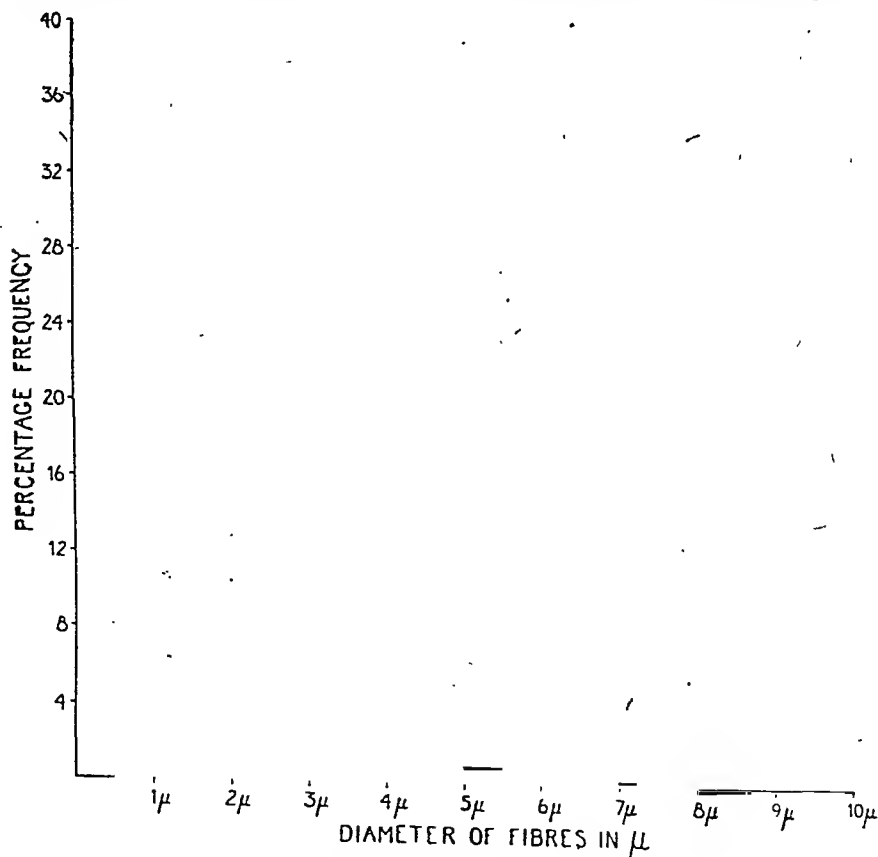


FIG. 2.

Histogram of the percentage distribution of about 4000 nerve fibres of various sizes in the human optic nerve



in somatic motor (Häggquist, 1937) and somatic sensory nerves (Szentágothai-Schimert, 1941), with the difference that the maximum is shifted to the left, showing a much higher frequency in the under- $2\mu$  range. It approximates more closely to the range and frequency in visceral nerves. There is a closer comparison, however, between the height and position of the maximum in the optic nerve histogram and that of the pyramidal pathway in the basis pedunculi which, as shown in the investigation of Szentágothai-Schimert, is due to the inclusion in it of cortico-pontine fibres. The picture of the ponto-cerebellar tract is also similar (Szentágothai-Schimert 1941).

The second much smaller maximum at about  $5-7\mu$  may also be significant in view of the possibility that these fibres are related to the larger cell layers of the lateral geniculate body.

Polyak (1942) has observed that the optic fibres proceeding from the periphery of the retina towards the optic disc are thicker than those from the macula. He also points out that the larger ganglion cells are more numerous towards the periphery of the retina and small ganglion cells towards the area centralis and that, generally speaking, the larger cells send out thicker axons than the smaller cells. The possibility may be conjectured; therefore, that the disproportionately large number of fine fibres in the human optic nerve (as compared with other mammals) proceed mainly from the small ganglion cells, possibly from the midget ganglion cells which are in the majority in the macula. The increase in the midget ganglion cells and their related midget bipolars and cones in the central area of the retina (Polyak 1942), the relative increase in the number of fine fibres of the optic nerve, and the remarkable increase in the number of small cells in the central vision area of the lateral geniculate body in the ascending phylogenetic series (Chacko 1948), appear to be consequent upon the differentiation of central vision. The higher frequency of fine fibres, the great number of monosynaptic connections and neurons of smaller size in contrast to thicker fibres, converging pathways and larger neurons are interesting features of the visual neural system. If the suggestion proves to be correct, that the nerve fibres forming the macular pathways from the retina to the cortex are of relatively smaller calibre, then the current idea that the relatively thicker and fast-conducting fibres convey impulses destined for the visual cortex, while the thinner slow-conducting fibres only reach the tectum, will need to be revised. However, increase of fibre diameter is only one of the factors related to a higher conduction velocity (Young 1946). An alteration of the histochemical properties of its sheath may have the same result. As is clear in Fig. 1, the fine fibres have a distinct myelin sheath, but there is a relatively greater thickness of myelin sheath in the finer fibres. The nature of the sheath in these fine fibres is well worth study with the technique of polarization optics and X-ray diffraction analysis. Histograms of the optic

nerve fibre-calibre in clinical cases of toxic amblyopia where the macular bundle is mainly affected, or in experimental lesions of the macula, and also a comparative study of the normal histograms in a series of primates and sub-primates, should throw further light on the subject; work along these lines is in progress.

I wish to thank Prof. W. E. Le Gros Clark for encouragement and advice while carrying out this work.

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## ACUTE RETINOPATHY WITHOUT HYPERPIESIS IN DIABETIC PREGNANCY\*

BY

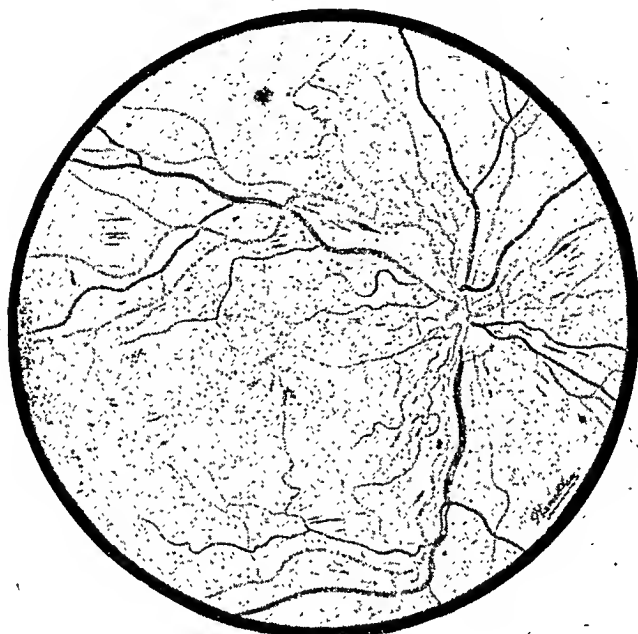
R. D. LAWRENCE

OF THE DIABETIC DEPARTMENT, KING'S COLLEGE HOSPITAL,  
LONDON

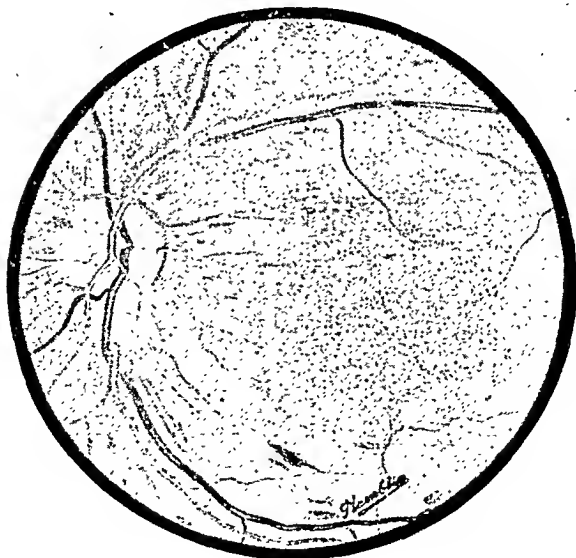
I HAVE recently seen acute haemorrhagic retinopathy in two pregnant diabetic women such as has not hitherto been described. Retinopathy is all too common in *long-standing diabetes*, but is a slow process with characteristic venous haemorrhages and exudates developing slowly over years, although a form which quickly develops into retinitis proliferans is occasionally seen. The severe *toxaemia* of *pregnancy* too produces an acute retinopathy with oedema, papillitis, severe haemorrhages, "albuminuric" in nature and appearance, always associated with hypertension, albuminuria and toxaemia. The following two cases fall into neither of the above categories, have not been described in ophthalmology or diabetic literature and presented a novel problem as to the termination of these pregnancies. The condition must be very rare and I have seen it in only 2 of some 200 diabetic pregnancies closely followed and is so striking in visual defect that I could not have missed other such cases.

\* Received for publication, March 19, 1948.

CASE 1. A very long-standing case who developed diabetes at age of 11 years in 1924, had insulin for 19 years before her pregnancy in 1943 at the age of 30 years. She was a spirited and clever young woman who led the wildest of diabetic lives, travelling all over the world on insulin varying from 20 to 80 units a day,



CASE 1.



CASE 2.

often loaded with sugar and ketones, precomatose from short supplies of insulin in the Tropics and a perfect candidate for retinal and other complications which long-standing and especially uncontrolled diabetes often brings. Married in 1942, after a miscarriage at 3 months, she again became pregnant and when seen at 10 weeks determined to co-operate in every way and rest and progesterone were followed. Her eye grounds and general physical state were normal. At 20 weeks, after a few days of mild sickness and vomiting, misty vision developed and when she was admitted for observation at the 23rd week, severe haemorrhagic retinopathy and a little exudate were obvious. Mr. Savin's notes gave the following details (December 1943). "Very extensive bilateral retinopathy with macular oedema and some exudate at L. macula. There are numerous flame-shaped and circular retinal haemorrhages. The vessels do not seem badly affected; no swelling of the discs. This is a serious haemorrhagic retinopathy. I could not be at all sure ophthalmoscopically if it were diabetic in origin and have no experience of the effect (nor necessity) of terminating pregnancy." (See Fig. 1.) Several other physicians and ophthalmologists confessed their ignorance. I had expected perhaps some renal toxæmia, but every urinary and blood test was normal (blood pressure 110/70 as always). After this her vision improved a little but when seen at the 30th week, her eye grounds were the same except for less macular oedema. After this, war conditions made London difficult and a healthy child was produced by Caesarean section in her home town at the 37th week. Her vision improved ("normal," she said) but one year later (1945) I saw two typical diabetic punctate haemorrhages, a big dilated venule, a small white exudate and some fading haemorrhages at the right macula. After another year (April, 1946) a report from Mr. N.-P. R. Galloway said that although her vision is 6/6, 6/5, her right fundus shows fine vitreous veils like commencing retinitis proliferans and the left, a few punctate haemorrhages, typical of diabetic trouble. Before this she again became pregnant, but abortion was induced. So a retinopathy still persisted, seemingly diabetic. When examined 18 months later, however, 5 years after the original lesion, the fundi were entirely normal.

CASE 2 had a very similar early history. Diabetes began at the age of 10 years in 1930, much insulin—60-80 units—often too much food and gross obesity. First pregnancy in 1943, normal child by Caesarean section, normal eyes.

A second pregnancy (1946) began normally and the eye grounds remained normal until "influenza" with 4 days' severe vomiting occurred at the 28th week, followed at once by "misty and spotty" vision. When seen a week later an intense haemorrhagic retino-

pathy was present and Mr. Savin reported: "She has a severe bilateral haemorrhagic retinopathy with numerous flame-shaped and deep haemorrhages and a little exudate. The peripheral arteries are in many instances narrowed and in a state of spasm. Discs normal. In my view this is a toxic condition rather than the type usually associated with diabetic retinopathy." However, all tests for toxæmia in blood and urine were normal, blood pressure 110/60, very slight anaemia, B.S.R. 34 mm./1st hour. RH factor positive, no atypical antibody. Arm capillary fragility normal. Altogether nothing abnormal was found except the diabetes. Vitamin K and B<sub>1</sub> were given in large doses. In the next weeks bilateral Bell's Palsy developed and the retinopathy became slightly worse (see picture by Messrs. Hamblin). Nausea and occasional vomiting continued. Termination was most seriously considered, but the mother instinct settled our problem by refusal. The vision fluctuated for better and worse, more haemorrhages, more and less oedema.

After Caesarean section at the 32nd week the vision became "normal" within a week and we watched the haemorrhages fade. Six months later Mr. Savin reported "the retinae and vessels are normal apart from some faint pigmentary patches and 1 or 2 crystalline deposits, relics of previous haemorrhages. But all this is a mere trifle."

I, however, saw *one* deep punctate haemorrhage, to me typically diabetic, in the left eye ground. But all the acute haemorrhagic process had certainly gone and the eye grounds had returned practically to normal. A year later the fundi were normal.

### Discussion

I have not been able to find any similar published cases. In contrast I have followed 3 pregnancies in 2 diabetic women who previously had slight retinopathy, a few haemorrhages and fleck exudates, and the course of pregnancy made no difference to their retinal condition. Also I have followed about 12 diabetic pregnancies complicated with renal toxæmia, usually mild, which showed no retinal changes.

The only common factor in these two pregnancies different from many similar long-standing cases was unusual vomiting. This certainly raises the venous pressure and might well put the extra rupturing strain on the venules which are known to be the weak point in the diabetic retinal system. It is to be remembered also that the intra-ocular pressure is certainly reduced by dehydration, this diabetic disturbance being present in all such states of vomiting in severe insulin cases. But even if these two factors are causal ones in this retinopathy, it is hard to see why the condition should

persist almost unchanged until delivery. So perhaps it is wise to report these two cases without explanatory hypothecation.

### Summary

Two cases of acute and severe haemorrhagic retinopathy are described in pregnant diabetic women. The condition does not conform either to usual diabetic or to toxic renal retinopathy and the latter was excluded.

I am indebted to Mr. L. H. Savin for close study and reports on the retinal changes.

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## CRATER-LIKE HOLES IN THE OPTIC DISC\*

BY

EMANUEL ROSEN

NEWARK, N.J.

ALTHOUGH Duke-Elder<sup>1</sup> has stated that the condition known as "pits" or "crater-like holes in the optic disc" is of relatively frequent occurrence, yet Greear<sup>2</sup> has been able to collect and tabulate only seventy-two cases including his three cases, the only three he had encountered in eighteen years of active practice. There would seem to be sufficient reason to report any additional cases and possibly in so doing to lend statistical support to the present-day concept of the condition without the necessity of awaiting pathological studies before one can be sure of the nature of this anomaly<sup>3</sup>.

CASE 1. This 31-year-old patient was examined routinely prior to embarkation. His vision was 20/20 in each eye and his only ocular complaint was difficulty in reading for prolonged periods. There were no abnormal eye findings other than those of the right disc (Fig. 1). This disc was ovoid in shape with a thin, pigmented scleral ring on the temporal side. There was present a small physiological cup about 1/3 D.D. in size located slightly upward and nasally. The cup was about three dioptres in depth and presented a pronounced cribriform plate at its bottom. Just nasal to the physiological cup was a triangular-shaped "pit" with its apex pointing inferiorly. This "pit" did not reach quite to the edge of the disc nor to the nasal edge of the physiological cup. The "pit" appeared to be blue-grey in colour and seven or eight dioptres in depth. A thin connective tissue veil seemed to be present within the cup rendering it difficult to visualize the bottom

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of this "crater." The edges of the "crater" were quite distinct. One small vessel could be seen approaching the nasal side of the disc and then disappearing over the nasal lip of the "pit." This vessel could not be followed very far down into the "pit" for it

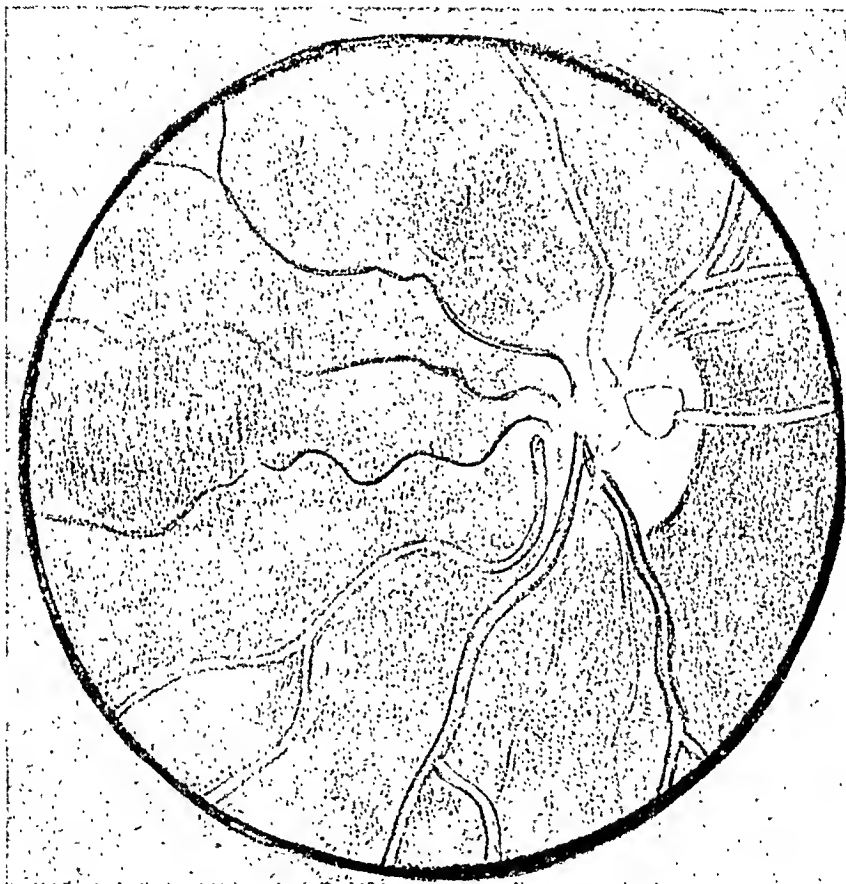


FIG. 1.

seemed to disappear completely. There was no further anomaly of structure of this disc. The patient's vision was found to be 20/20 in each eye with correction. Fields and blind spot studies produced the pictures seen in Figs. 2 and 3.

In summary this disc presented a "pit" upon the inferior nasal aspect of the disc triangular in shape and seven or eight dioptres in depth. A temporal crescent was present along with a characteristic field defect. The "pit" was covered over by a connective tissue substance and was blue-grey in colour.

CASE 2. The second case was that of an adult male, aged 51 years, who appeared for a routine refraction and offered the information that he had upon a previous examination been informed that there was present in his right eye a very rare condition known as a "hole in the optic nerve." After learning of this condition the

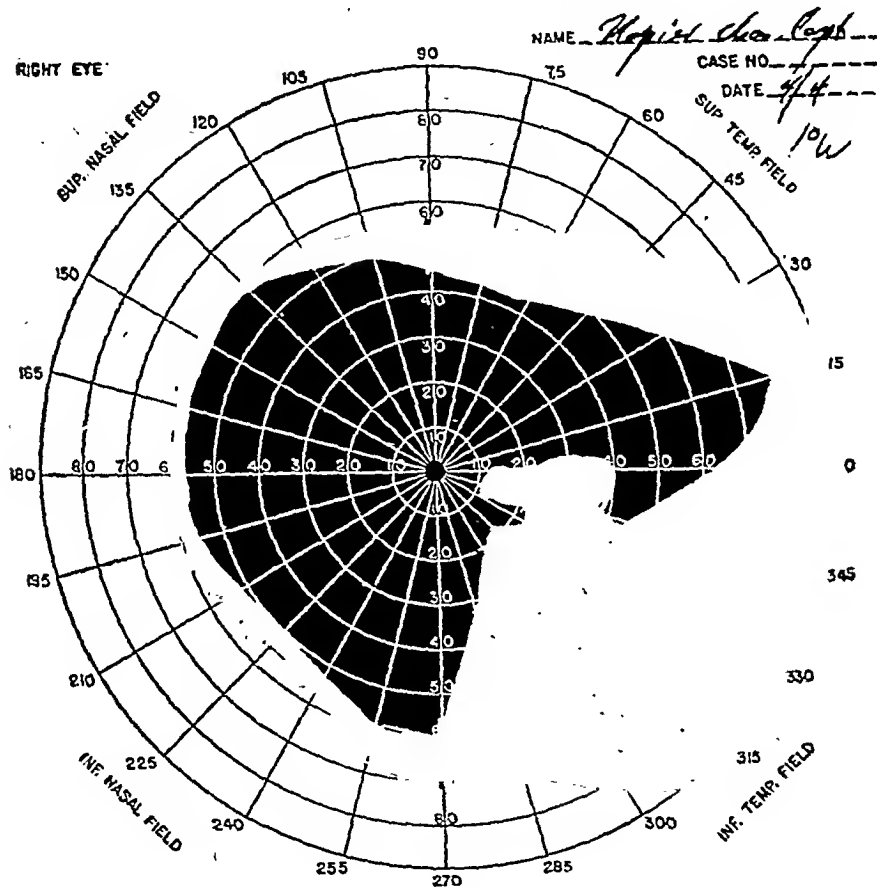


FIG. 2.

patient had conducted several tests upon himself in which he learned that he had a field defect in his right eye which to him seemed quite marked when compared with the visual field of his left eye.

Examination of the left eye was not remarkable. The right eye too was not unusual, except for the appearance of the right disc (Fig. 4). This showed a pigmented greyish-black scleral crescent upon the nasal third of the disc which was fairly well demarcated in its upper half but not pigmented below. There were three islands of clear area within the crescent. A fairly large physio-



logical cup was present which occupied about one-third the entire area of the disc and was eccentrically displaced nasally. The central retinal vessels emerged in no unusual manner from this cup with the primary arterial and venous bifurcation occurring before emergence. On the temporal portion of the disc a very small round "pit" was present which approached but did not

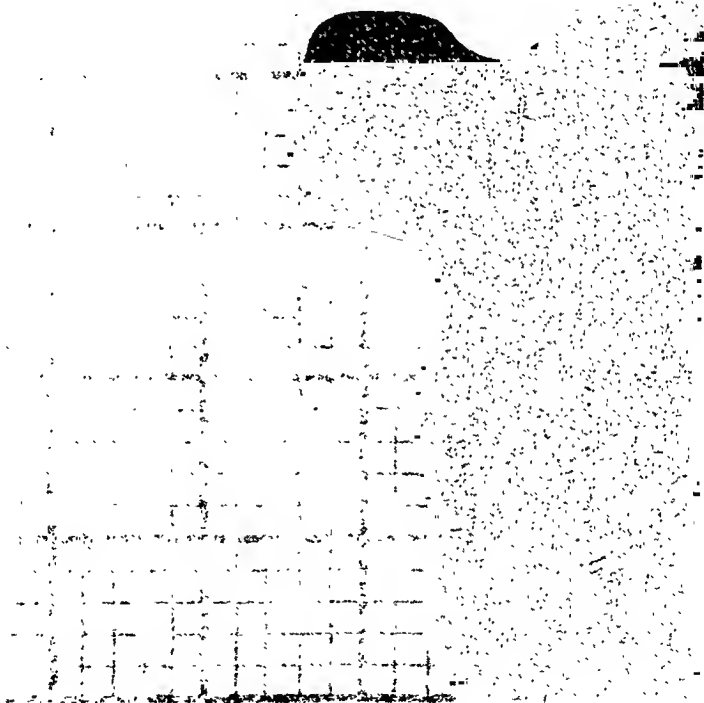


FIG. 3.

touch either the physiological cup or the disc margin. One small vessel appeared to enter the cup near the upper edge, emerging at approximately "9 o'clock" and running upward over the disc edge. Below the lower lip of the "pit" a small vessel approached the edge of the hole but then curved gracefully away to run off the disc and on to the retina. The "pit" was of pale blue colour and was covered over by a greyish foam-like membrane so that the depth of the hole could not be ascertained. The hole seemed to

take a slightly oblique source temporally. There were no other anomalies of the vessels upon the disc or the retinal structures. A study of the visual field disclosed a defect as pictured in Fig. 5.

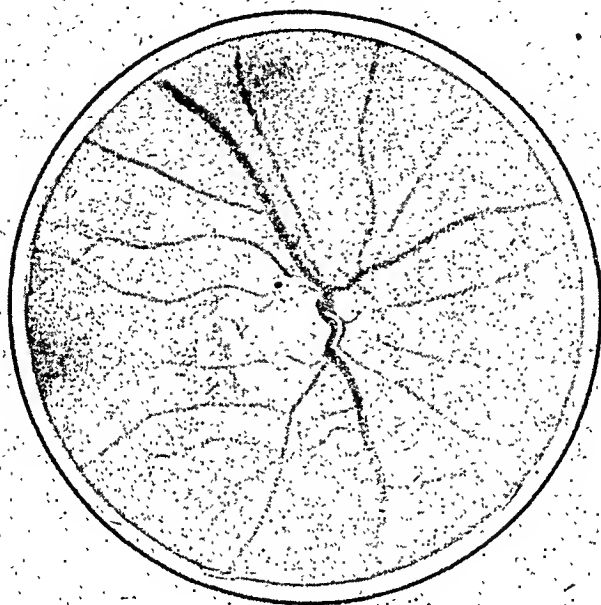


FIG. 4.

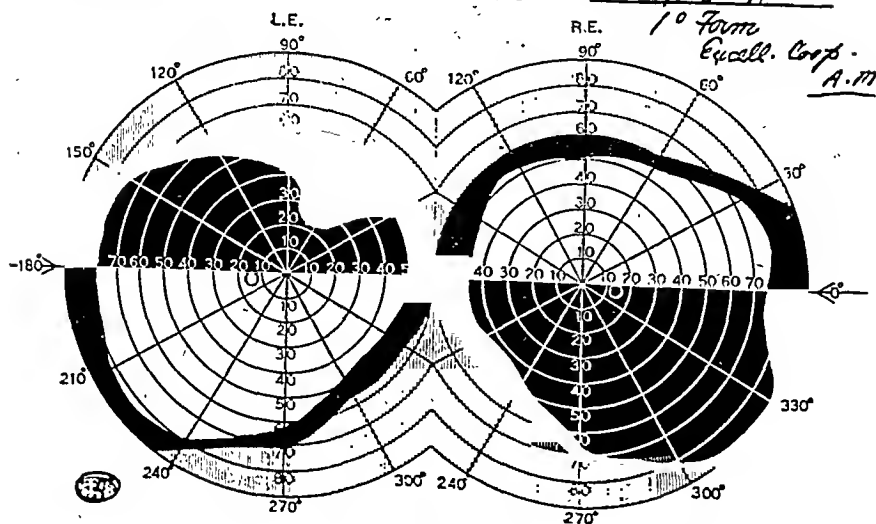
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FIG. 5.

CASE 3. This patient, aged 29 years, was examined at this hospital because of extremely poor vision in his right eye of many years' duration. This eye had always been much poorer than his left eye and although the patient was right-handed he was aware of the fact that he had always used his left eye when sighting through a rifle. About ten years ago the right eye was injured by a small seed brushed from some tall grain. The patient was seen shortly afterwards by a specialist who removed a foreign body from the cornea and then put a patch upon his eye. When this patch was removed the patient noticed that his vision was greatly reduced. He doesn't recall making any effort to determine the cause of this diminished vision subsequently, but knows that at every eye examination thereafter something of interest was discovered in his right eye which caused a good deal of comment by all examiners. Examination disclosed vision in the right eye to be restricted to hand movements. The external ocular examination was negative. The right eye was slightly divergent; no effort was made at fixation. The iris and lens were normal. In the right macula there was a horizontal lesion resembling a tear with the prominent redness of the choroid brightly shining through and with the edge of this cleft strongly pigmented. There was a definite and complete scleral temporal crescent and in the infero-temporal portion of the disc was an obliquely placed slightly triangular



FIG. 6.

"pit" (Fig. 6). This was about  $1/8$  D.D. in size and was covered over by a rather dense connective tissue membrane which was somewhat shiny. The "hole" was greyish-blue in colour; its depth could not be measured since one could not focus beyond the range of the connective tissue covering. The temporal edge of the "pit" did not quite reach to the edge of the disc. Its margin temporally was extremely distinct and the oblique nature of the "pit" appeared to be emphasized by this sharp temporal edge. In the inferior portion a vessel seemed to approach the hole and then pull away from it without entering the "pit." There was a pronounced physiological cup with normal vessel arborization. A visual-field study done upon this eye failed to illustrate the characteristic sector-shaped defect probably because of the extremely poor fixation resulting from the macular lesion. There was a marked concentric contraction of the peripheral field.

CASE 4. Is that of an adult male soldier 27 years who had been under the care of the eye department at a station hospital for more than a year because of suspected glaucoma. During a routine examination for refraction the peculiar cupped appearance of the patient's left disc was observed (Fig. 7). Following changes noted in the blind spot of that same eye, the patient was put upon an anti-glaucomatous régime. He was observed at very frequent



FIG. 7.

intervals during which time no variation was discovered in the appearance of the blind spots, the peripheral fields or the diurnal tension curve. Vision in each eye was 20/70 but was readily corrected to 20/15. There was no involvement of the peripheral field but studies of the blind spots showed an enlargement (Fig. 8



FIG. 8.

The fundus of the right eye presented a small colobomatous area just below the disc enclosed by a pigmented crescent and traversed by several retinal vessels which certainly suggested the presence and location of an atypical congenital coloboma (Fig. 9).

CASE 5. A. S., aged 10 years, had been given occlusion therapy because of an amblyopic left eye. This consisted of total occlusion during the summer months and occlusion therapy several hours daily after school. The treatment was continued for a period well

over one year at the end of which time no improvement was noticed. The patient was first seen shortly thereafter. During routine fundus examination a crater-like "pit" in the optic disc



FIG. 9.

of the left eye was noted in the inferior temporal sector of the disc. It was oval in shape, greenish-grey in colour and apparently quite deep, although the depth of the "pit" could not be ascertained both on account of the connective tissue overlay and the obliquity of extension of the hole. Two small vessels approached this crater and then dipped very abruptly over its edge to disappear into its depth. A rather pronounced physiological cup was present in this disc (Fig. 10).

CASE 6. This patient was a 47-year-old female who recently developed symptoms of presbyopia. She had never suffered from any eye condition. There were no irritative phenomena, headaches or blurred vision. Within the past six months difficulty in threading a needle and in reading telephone type had become more and more pronounced. The patient's vision was 20/25 in each eye and was readily corrected to 20/20 in each. The right pupil was smaller than the left. Although each pupil reacted to light and to accommodation, the response of the left pupil was not very prompt to light. There was considerable atrophy of the inner circle of the



FIG. 10.

iris of the left eye with a very mild degree of iris atrophy on the right side. The media were clear. The fundus of the right eye appeared perfectly normal. The left fundus presented the anomaly shown in the fundus photograph (Fig. 11). The fundus in general was albinoid with the choroidal circulation readily showing through to the retina. The disc was slightly oval in shape with the upper four-fifths appearing quite normal in all respects but the lower fifth presented an anomalous depression. This lunar-shaped depression was five dioptries in depth, greyish-green in colour and covered by a thin irregularly-formed veil. On the temporal side two vessels disappeared suddenly just beyond the margin of the cup to become visible again in the depths of the depression. On the nasal side one large vein was seen dipping abruptly into the cup and reappearing just beyond the margin of the disc. The vessel pattern was not particularly abnormal. Because of the irregularity in the size of the pupil, the atrophy of

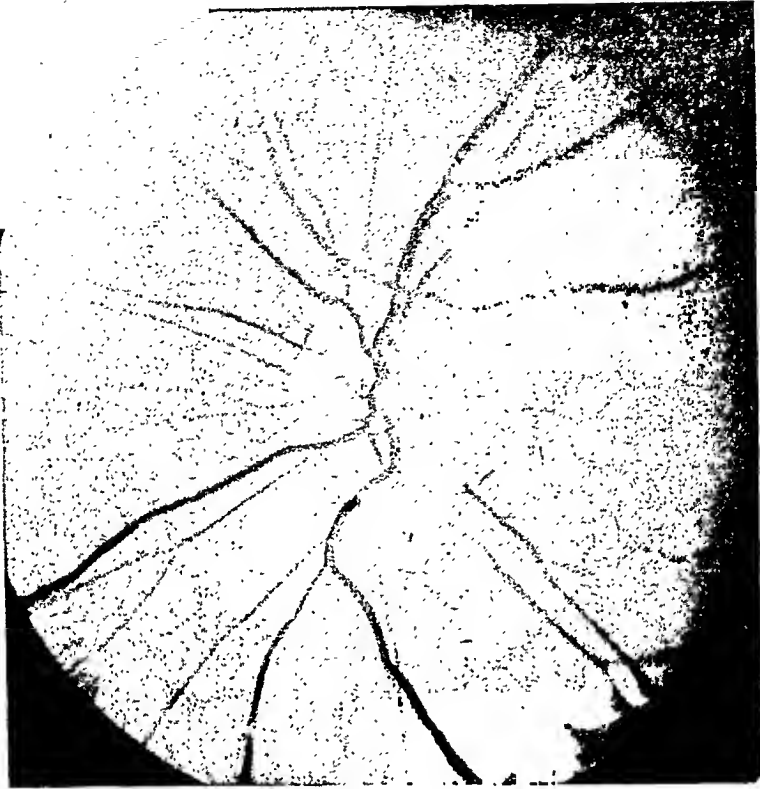


FIG. 11.

the iris, the appearance of the left disc and because of lack of familiarity of the condition of "pits" a study was made of the patient's intra-ocular pressure, but the diurnal curve failed to show any variation of significance. Provocative tests (*i.e.*, dark room, dilatation, coffee, excess of fluids), caused no increase in the intra-ocular pressure. Studies made upon visual fields and blind spots showed a defect associated with the congenital "pit" (Fig. 12).

CASE 7. This 42-year-old female first sought aid because of persistent diplopia, headaches, nausea and vomiting. For many years she had been able to read only if one eye was kept closed. She also noticed that the left lid had a tendency to droop, the condition becoming quite pronounced when she gazed into the mirror. The patient was found to have a paresis of the left superior rectus muscle along with a pseudoptosis. The fundus of the right eye appeared normal. The fundus of the left eye showed a peculiar cupping of the nerve head. In the lower outer quadrant there was a small partial coloboma about  $1/8$  D.D in size and slightly bluish



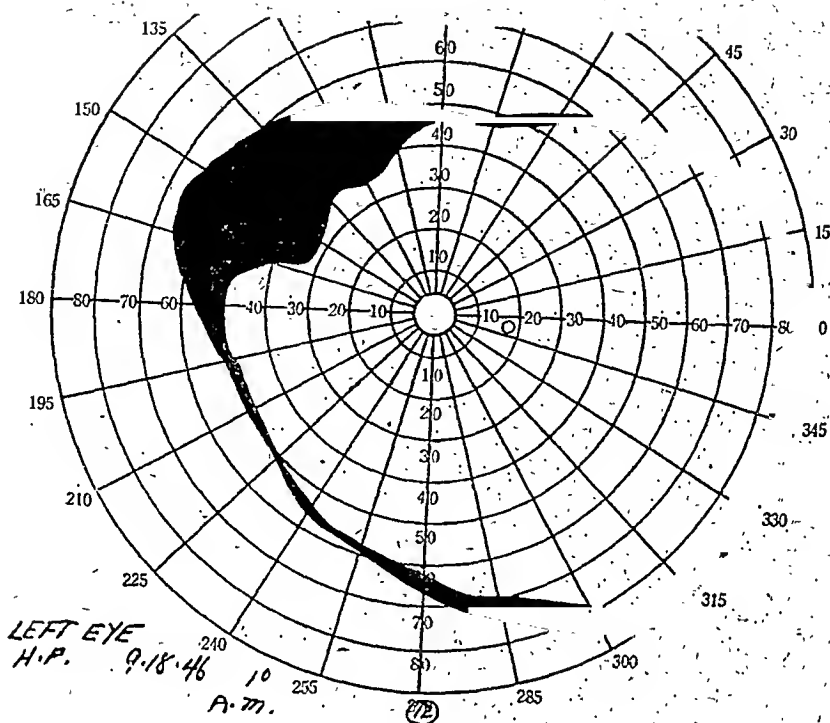


FIG. 12.

in colour. It was covered over by a connective tissue membrane so completely that no depth could be determined for the hole formation.

### Discussion

Most case reports of this condition show the crater to be present in the temporal half of the disc and usually in the lower portion. The "pit" never extends beyond the edge of the disc although that structure may be distorted in a horizontal direction. A. Fuchs<sup>2</sup> stated that congenital "pits" occupy the sclera adjacent to the lower margin of the papilla and only exceptionally are they seated within the papilla itself. Fuchs presented a very rare case in which a congenital "pit" was within the excavation of a glaucomatous cup. Most "holes" appear to be directed backwards in a straight and not an oblique fashion. Cases 3 and 5 in our series appeared to be somewhat oblique. Also in Case 3 the temporal margin of the disc appeared to be unusually sharp. In three instances the depth of the "pit" could not be ascertained in our cases; in case 1 the "crater" was seven or eight dioptres in depth. In a case reported by Moffatt<sup>4</sup> it was noted that the darkest part of the

hole was at its outer edge giving the impression that the deepest portion of the "pit" was behind the overhanging edge of the sclera. This same appearance was also noticed in our third case. In a case reported by Neame<sup>5</sup> the patient noticed a gap in his visual field which caused him to seek aid much as occurred in our second case. Mann<sup>6</sup> states "there are no vessels in the pits," which statement is apparently not true, for in a case reported by Nielson<sup>7</sup> the author states that "vessels descended at the edge of the groove and reappeared upon the other side." Several of our cases also show vessels within the "pits."

A case presented by G. Edmund<sup>8</sup> showed a groove which occupied the entire temporal half of the disc and reached completely to its margin. This groove was darker in colour but only three dioptres in depth. A second case reported by this author showed an inferior conus with a horizontally oval hole lying between the disc and the crescent. This second case had iridodonesis which was pointed out as a factor in suggesting that the condition is one of congenital abnormality. Other anomalies are said to be associated with this condition—i.e., microphthalmia, ectopia lentis, coloboma, persistent hyaloid artery, etc—but none was observed in our case reports.

Most authors believe the "holes" are colobomata. They may be the result of defective foetal cleft closure, or a remnant of the hollow which connects the optic cup with the cavity of the optic stalk. Wessely<sup>9</sup> believes the "pits" are remains through which have passed cilio-retinal or optico-ciliary vessels whose atrophy had been completed rather late in intra-uterine life. Edmund<sup>8</sup> thinks the "pits" are the results of abnormal vascular grooves. Alabaster<sup>10</sup> expressed the opinion that a vascular accident caused a collapse of the small capillaries in the nerve head with a defect subsequently remaining. Mann<sup>6</sup> states that in all probability these defects are *not* holes, believing that their nature is not always clear since they seldom come to microscopic examination. She furthermore states they may be cysts or pockets filled with transparent tissue, but there is no clinical evidence that these structures are cystic. Greear<sup>2</sup> has emphasized that the condition is not a true coloboma which would be secondary to disturbance of closure of the foetal fissure. He states that these "pits" are atypical colobomata by which is meant that the "pit" resembles a coloboma but has its origin in an entirely different manner.

**SUMMARY.** Crater-like holes may be erroneously regarded as evidence of glaucomatous changes, particularly when there are pupillary inequalities, iris atrophy and field defects. They may also be present in amblyopic eyes in which instance, recognition

should lead to avoidance of occlusion therapy. The field defect may be quite constant and may be recognised by an observant patient. Case 4 would tend to strengthen the belief that the condition is a congenital one. The possibility of such a "pit" extending back into the orbit and uniting with a cyst, thus producing unilateral exophthalmos, should also be borne in mind<sup>12</sup>.

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## A CASE OF A GRÖNBLAD-STRANDBERG SYNDROME, WITH DISCIFORM DEGENERATION OF THE MACULAE\*

BY

GEOFFREY HIBBERT

ASST. HON. OPHTHALMIC SURGEON, SWANSEA  
GENERAL AND EYE HOSPITAL

IN March, 1946, C. R., male, married, aged 38 years, a motor salesman, noticed distortion of objects to his right side, most noticeable when he was car driving, and absent when he closed his right eye. At that time, his visual-acuity was 6/5 6/5 (Snellen) with no error of refraction and at six metres, there was  $\Delta 1\frac{1}{4}$  left hyperphoria, and at 20 cms. esophoria 3°. The media were clear, but each fundus showed several, small, scattered, ovoid patches of yellow-white exudate with discrete, faintly pigmented margins, two of which were in the right macular area. Over these, the macular capillaries were without distortion or interruption.

During one year, the case was repeatedly examined, and several, new, small patches of exudate were seen to form in the mid-periphery of each eye.

In March, 1947, several new patches were seen in the right

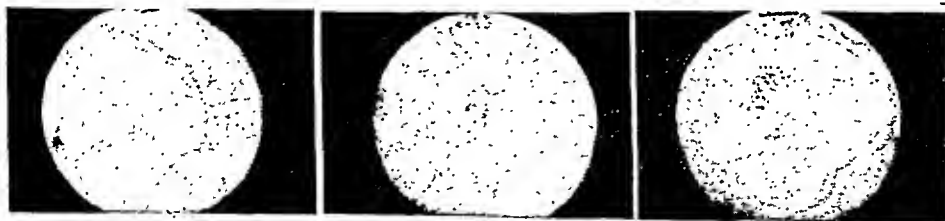
\* Received for publication, March 11, 1948.

macular area, and subjective testing on Bjerrum screen at two metres revealed a scotoma in the right central area of the field of vision, with a dense nucleus and sloping edge which overlapped the fixation point. The vision of this eye was reduced to 6/24 by April, 1947.

The case was observed closely, and in September, 1947, the patient reported rapid failure of central vision for all purposes, including close work during one week. He was unable to read newsprint, and objects seen with the left eye appeared distorted and blurred. Visual acuity was then O.D. less than 6/60; O.S. 6/36 partly.

The scotoma, recorded before as present in the right central area, was found on Bjerrum screen at two metres, to be more extensive, with a larger, dense nucleus and steeper margins. The scotoma was dense to targets of less size than 10/2000 white (artificial light 100 watt 6 feet above patient). The left field of vision showed a small, central scotoma, relative in quality.

The right fundus, at this time, showed a roughly circular, white patch of exudate in the macular area, approximately twice the size of the optic disc, over which the macular capillaries ran without distortion, though standing out well against the brilliant white background of exudate. This patch gave the impression of being slightly-raised above the level of the surrounding normal retina. To the nasal side of the disc, a brown-black angiod streak was



PHOTOGRAPHS 1-3.

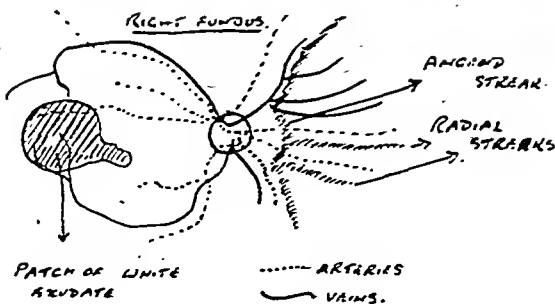


DIAGRAM 1.

present with indistinct powdery margins, equal in width to an artery of first division of the central retinal artery, and curved concentrically with the disc margin, separated from this by a narrow interval. Three angeoid streaks ran radially from the convex border of this out towards the nasal mid-periphery of the fundus. (See photographs 1-3 and diagram 1.)

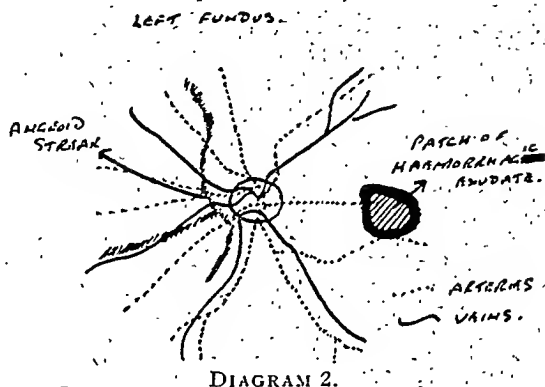


DIAGRAM 2.

The left fundus showed a "haemorrhagic" patch of exudate, roughly circular, in the macular area, and one half the size of the optic disc. This patch increased in size from day to day, becoming constant at the side seen in photographs 4-5 and acquiring a grey-black centre and brown-black margin, as is well seen in the photographs as two separate densities.



PHOTOGRAPHS 4-5.

An angeoid streak was present in the left eye, similar in appearance to that in the right fundus, but placed nearer to the disc margin on its nasal side.

On each fundus, the retinal vessels were normal in appearance, while the patches of exudate in the mid periphery of each fundus were not related to the radial angeoid streaks. The retinal vessels crossed the angeoid streaks without deformation or distortion.

Throughout the period of observation, no signs of uveitis have

appeared, with absence of "K.P." aqueous or vitreous haze, and ciliary injection, while the fields of vision remained of normal, relative extent.

A discrete patch of pigmentation on the anterior surface of the right iris has remained unaltered.

During the period of observation, it was noticed that the patient had altered skin of the left side of the neck. Similar changes were found on extensive areas over the epigastrium, lower chest anteriorly, the anterior fold of the left axilla, and the skin of each antecubital fossa and axilla. In all these areas, the skin was soft, thin when picked up between finger and thumb, excessively mobile on the underlying tissues, and possessed a fine mosaic of yellow ridges, less than a millimetre in width, easily palpable to the pulp of the examining middle finger. The effect of voluntary contraction of platysma myoides on the skin of the neck was less on the left side than on the right. One café-au-lait stain, the size of a British penny postage stamp, was present over the left temporal region.

### Investigations

*March, 1946.*

	$\frac{1}{1,000}$	negative
Mantoux intradermal skin test	$\frac{1}{10,000}$	negative
	$\frac{1}{100,000}$	negative

Wassermann (venous blood), negative. B.P. 160/70. Chest X-ray.—No abnormality seen. X-ray teeth.—Apical infection of two teeth. These were extracted.

*September, 1947.*

X-ray paranasal sinuses.—"Loculated type of antrum on the right side, with diminished translucency of part of the antrum. ? Congenital anomaly ? after infection." There are no clinical signs or symptoms of antrum disease.

*October, 1947.*

X-ray skull and pelvis.—"There is no evidence of Paget's disease of bone."

B.S.R. 3mm. in one hour. Coagulation time, 2 mins. 40 secs. Bleeding time, 7 mins. 30 secs. Hb. 92 per cent. R.B.C.'s, 5'06 million. C.I. 0'92. W.B.C.'s 12,600. Polymorphs 62 per cent. Eosinophils 1 per cent. Basoph 1 per cent. Lymphocytes 30 per cent. Mononuclears 6 per cent. The red cells were of normal shape, size and staining. Capillary fragility test.—Slight increase.

Urine.—No abnormal constituents.

V.—O.D. less than 6/60. O.S. 6/60, with  $-0.50$  D.Sph. added—part of 6/36; eccentric fixation—part of 6/24.

The patient readily and suddenly learned to appreciate the value of fixing slightly to one side of the object of regard.

Telescopic lens systems. (Hamblin's). O.D. 6/60. O.S. 6/36 with  $-1.00$  D.Sph. placed behind the system.  
part of 6/24 direct fixation.  
6/18 eccentric fixation.

With a  $12$  D.Sph. small lens added to the system. O.D. J.16 read badly. O.S. J. 10 read rapidly and well.

General physical examination showed no abnormal signs, radial pulses equal and normal, 72 per min. There is no history and no other sign of peripheral vascular disease except a history of pain in both calves after walking about a mile or so. This pain subsides after resting, but is inconstant in incidence.

*Family History.*—The father and mother died aged 75 years and 77 years respectively, and one brother died as a youth of tuberculous peritonitis.

One sister has normal vision, and the patient knows of three cousins with no history of eye disease, though none was available for examination.

*Diagnosis.*—When the case was first seen, the diagnosis was disseminated choroiditis, using the term in a descriptive sense, rather than the narrower sense of implying the common picture of syphilitic choroiditis.

The significance of the angeoid streaks was clearly recognised and a bad prognosis given.

The skin condition was not discovered until September, 1947. The patient gives a long history of unusual skin texture in the areas described, with no recent change.

The changes in each macular area have been labelled disciform degeneration, and the photographs show perhaps two stages in a common process, the right eye a late stage, the left an early "haemorrhagic" state.

*Treatment.*—Focal sepsis was searched for, but, apart from the teeth mentioned, none was found.

Sulpha drug, penicillin, mixed vitamins, iodides, salicylates, coagulin ciba, and other drugs have been given a trial, but the case has steadily progressed to the present state.

### Photographs and diagrams

*Comments on Photographs.*—These photographs stress the severe limitation of fundus photography as so far evolved. In them, the size of the areas of macular exudate is shown, and

the difference in appearance on the two sides is also shown well. The angeoid streaks are recorded but faintly and appear similar in the one side on photographs 1 and 2—as opposed to obvious defects and artefacts which have moved in position on the two photographs.

The arteries and veins of the same fundus differ in different photographs in apparent diameter and appearance. This illustrates my personal opinion that fundus photography cannot be held to record accurately such factors as the nature of the light streak, arterio-venous crossings, venal diameter, though the degree of tortuosity (or “straightness”), especially of macular capillaries, can be recorded thus.

This opinion I have reached after photographing a series of 150 fundi in healthy persons of greater age than forty years.

The Grönblad-Strandberg syndrome consists of angioid streaks of the fundi with pseudo-xanthoma of the skin. Originally described by Grönblad, with Strandberg as the authority on the skin condition, this syndrome has been repeatedly found and cases published.

The existence of other abnormalities has been found in the presence of the syndrome, or of the angeoid streaks.

The syndrome, plus exudation at the macula resembling disciform degeneration, was described by Goedbloed<sup>2</sup> who quotes Wildi, 1926, as describing three stages of development of the lesion in the macular area.

1. Streaks with normal central fundus.
2. Detachment of the retina by exudate in the macular area.
3. Organisation of the exudate to form a grey disc.

The case described falls broadly into this description.

Angeoid streaks and senile elastosis of the skin are associated in two cases by Goedbloed<sup>2</sup>.

Angeoid streaks and Paget's osteitis deformans of bone have been described by Terry<sup>3</sup>, Lambert<sup>4</sup> and others<sup>5</sup>. The syndrome, however, has not been described in the presence of Paget's disease.

A case of moderately advanced Paget's disease was observed by me over a period of twelve months, and developed scattered small areas of yellow exudate in both fundi, some in the central areas. There were no skin changes in this case, and no streaks. The familial tendency of streaks has been established by Law<sup>9</sup>, Wassenaar<sup>10</sup>, Goedbloed<sup>2</sup>, who quotes Franceschetti, and Roulet, 1936, and the factor appears to be recessive.

Pathological studies by Hagedoorn<sup>5</sup> suggested degeneration of elastic tissue of Bruch's membrane, with perhaps similar alteration of the elastic structure of blood vessels. Law<sup>9</sup> found folding of the



retina and accumulation of pigmented debris to coincide with the streaks.

Recently, attention has been given to the blood vessels of the extremities in cases of angeoid streaks by Guenther<sup>6</sup> and Scheie<sup>7</sup> with Freeman<sup>7</sup>. Guenther investigated pulse wave velocity and form in the peripheral musculo-elastic arteries (*Muskelelastische Arterien*) in nine cases of the syndrome, eight of arteriosclerosis, and nineteen "normals." The velocity was lower in the syndrome cases, while the proportion of the height of the base of the incisure, compared with the amplitude, expressed as a percentage, was higher than normal.

The alterations found were considered significant, and indicative of degeneration of the elastic tissue elements of the vessel walls. There was no confirmation by biopsy of the vessels. Symptoms attributed to vascular changes were weakness of extremities, coldness of hands and feet, dyspnoea. Scheie<sup>7</sup> and Freeman<sup>7</sup> supply some confirmation in describing three cases of streaks. In two cases, the whole syndrome was present, with severe vascular disturbances in the limbs. Absence or diminution of pulsation of peripheral arteries was present. Oscillometric records of pulsation showed a generally diminished amplitude in these vessels in both cases. In one case, biopsy of an ulnar artery was carried out. The diminished pulsations were confirmed during the dissection.

Histologically, the intima and internal elastic lamina were normal. The media showed fragmentation and vacuolation of elastic tissue by Weigert's stain to a marked degree. There was hypertrophy of muscle fibres.

In both cases showing vascular abnormalities, calcification of major limb vessels was evident radiographically. These writers suggest routine ophthalmoscopic examination of cases of unexplained peripheral vascular disease.

The association of Paget's disease with the angeoid streaks, angeoid streaks with changes in the dermal elastic tissue, the streaks and skin changes with peripheral vascular disease, and with abnormal calcification of peripheral major vessels, point to a probable common factor. Perhaps more systematic investigation of each type of case may be productive of further knowledge, but the tendency for each writer to be confined to a small collection of each manifestation operates against this.

Permission to publish the account of this case by Mr. J. J. McCann, F.R.C.S., of Liverpool, under whose care the case was observed, is acknowledged. Use of the fundus camera at the Liverpool Medical Research Institute was granted by the Director, Dr. I. Harris, Liverpool.

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## A MYXO-HAEMANGIOMA SIMPLEX OF THE CONJUNCTIVA BULBI\*

BY

A. BAKKER

GRONINGEN

A WOMAN, aged 35 years, came into my consulting-room, complaining that she had the sensation of a foreign body in her right eye. For six weeks she was aware of the presence of a small tumour in the inner angle. Nothing was known about any trauma. The tumour was growing rapidly and at the time of my investigation it was about 4 mm. high and had a diameter of 3 mm. It was of a fungus like shape and had a broad and short pedicle. It was movable on the underlying tissue. Its base was partly covered by the semilunar plica. The tumour had a cherry-red colour and a smooth surface. At its base a tortuous and dilated vessel was visible.

Because of its disfiguring effect and its rapid growth I decided to remove the tumour. This was performed under cocaine anaesthesia. The tumour was excised by the single snip of a pair of scissors. There was little or no haemorrhage. Fixation with Bouin's liquid.

The microscopical examination gave the following picture: The whole tumour is completely covered with normal epithelium, containing many goblet cells (Fig. 1). The main substance of the tumour consists of compactly arranged small blood-vessels (dilated capillaries). The endothelial cells are extremely swollen. Here and there we find more than one layer, so that the lumen is obliterated by them. Some larger vessels intersect the tumour. In various sections we see large oedematous areas and some smaller

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FIG. 1.

interstitial haemorrhages, probably the result of interference with the blood circulation. The anatomical substrate of the impairment of the normal blood supply we see in the thrombotic vessels in the tissue subjacent to the tumour (episclera). At the same time these clotted vessels give us the explanation of the fact that the excision of the tumour caused practically no haemorrhage. The tumour is surrounded by a thin fibrous capsule. The connective tissue in the tumour is very poorly developed. In the sections, stained after Mallory, we see only an extremely delicate network of blue fibres round the capillaries. At many places several free macrophages are visible. They are loaded with pigment granules, being the result of incorporated red blood-corpuscles. Also some plasma-cells are present. At the base of the neoplasm, outside the capsule, we notice a lymphocytic infiltration under the epithelium. At the periphery of the tumour, but inside its capsule, we see a large jelly-like, oedematous area with a great number of spindle-shaped cells, which constitute a wide-meshed network. Most of these cells are unmistakably sprouting endothelial cells, but among them we also find young fibroblasts, which give rise to the formation of a meshwork of delicate connective tissue fibres. The homogeneous substance lying in the meshes gives a positive mucin-reaction with thionin. It is this area where the tumour obviously shows signs of an intensive growth, but also the mitotic figures in the depth of the tumour give evidence of a constant proliferation. With these symptoms the rapid growth of the neoplasm is fully explained.



FIG. 2.

In Figure 2 we see under a higher magnifying power a tangentially cut section of the tumour, just outside the pedicle. The above-described reticular tissue, consisting of young fibroblasts and proliferating endothelium-cells, can be distinctly seen.

Coming to the point of making a diagnosis, we may say that in the underlying case we have to do with a haemangioma simplex of the conjunctiva bulbi, which simultaneously shows signs of an intensive proliferation and a myxomatous degeneration.

### Discussion

Pedunculated haemangiomas of the conjunctiva bulbi are very seldom described in the ophthalmological literature. This is the reason that I thought it worth while to publish this case.

Among a great number of polypoid tumours of the conjunctiva which Elschnig<sup>1</sup> collected from the literature, he did not find typical angiomas with certainty. In a survey Pergens<sup>2</sup> reviews 52 cases of conjunctival haemangiomas (including two of his own). The majority of the tumours of the conjunctiva bulbi were situated in the inner angle of the eye. None of them resembled the neoplasm of my case. James and Trevor<sup>3</sup> report on two cases of haemangioma simplex arising from the palpebral conjunctiva. Their second case perhaps resembles somewhat the tumour in my case, but there is certainly a striking difference in the amount of connective tissue, which was in my case practically absent, so that the capillaries with their swollen endothelial cells were lying almost immediately next each other. Pendleton White<sup>4</sup> gives a description

of a capillary angioma arising from the palpebral conjunctiva of the upper eyelid. Here the convoluted thin-walled vessels were embedded in great masses of lymphocytes.

Maxted<sup>5</sup> describes a pedunculated angioma of the conjunctiva of the upper eyelid, which perhaps shows some resemblance to my case.

Summarizing we can say that a tumour similar to the fungus-like haemangioma of the conjunctiva bulbi in my case, has not been previously described. The fact that symptoms of intensive growth synchronised with myxomatous degeneration is noteworthy:

After eight months no recurrence has followed.

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## THE PROGNOSIS OF RETROBULBAR NEURITIS\*

BY

W. F. TISSINGTON TATLOW

MEDICAL REGISTRAR AND TUTOR IN MEDICINE,  
UNIVERSITY OF BRISTOL

VARIOUS theories as to the aetiological factors concerned in the production of retrobulbar neuritis have been postulated from time to time. In the days prior to the Wassermann reaction, a large number of cases were considered to be syphilitic in origin, and further evidence for this aetiology was given by a good response to mercury therapy. We now know that most cases of retrobulbar neuritis clear up rapidly without treatment. English authors have regarded disseminated sclerosis as the commonest cause of retrobulbar neuritis: Buzzard (1930) quotes Gowers as saying that gout is the next most frequent cause after disseminated sclerosis.

Marcus Gunn (1904) listed the following as possible causes in a series of 380 cases (tobacco amblyopia being excluded):—Periostitis 40, exposure to cold 27, dental sepsis 17; nasal sepsis 42, gumma 16, disseminated sclerosis 51, influenza 27, gout 22, varied (ptomaine poisoning, malaria, and constipation) 63, obscure 58, and the proportion of men to women was in the ratio of 31:27.

Marchesani (1936) in Bumke-Foerster's *Handbuch der Neurologie* lists the following figures: tumour (anterior fossa) 6, toxic 15, lactation 2, nasal sepsis 9, lues 24, disseminated sclerosis 113,

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encephalitis 7, meningitis 3, subacute combined degeneration 1, haematomyelia 1, vascular 4, tower skull 2, trauma 4, melaena 1, Mikulicz' syndrome 1, tenonitis 1, obscure 89.

Various factors have been definitely shown to produce retrobulbar neuritis other than those already mentioned. Amongst these must be included that of Cone (1938) and phenylalanine hair dyes described by Keschner and Rosen (1941).

Disease of the nasal passage and sinuses has been regarded as a potent cause of retrobulbar neuritis and operations on the sinuses were frequently advised. However, Traquair (1930) thought that all cases of idiopathic retrobulbar neuritis were probably due to disseminated sclerosis and that operation on the sinuses should not be performed. Chambers (1947), too, states that a series of cases of retrobulbar neuritis which he and Foster Moore examined showed no difference in prognosis whether the sinuses were operated on or not. Most neurologists now consider that disseminated sclerosis is the commonest cause of retrobulbar neuritis.

The incidence of a previous blindness in one or both eyes in patients with multiple sclerosis has varied according to the author concerned: Behr (1924) gives 75 per cent., Adie (1930) 30 per cent., Benedict (1942) 15 per cent. and Lillie (1934) 15 per cent. The percentage of cases of retrobulbar neuritis showing evidence of disseminated lesions at the time of blindness was 34 per cent. in a series of 34 cases recorded by Adie (1932).

Few cases have been followed up over a long period to ascertain how many later developed neurological lesions elsewhere. Bruns-Stolting (1900), Fleischer (1908), Langenbeck (1914), Marburg (1920) all state that varying percentages of patients with retrobulbar neuritis "later" developed abnormal neurological signs indicative of disseminated sclerosis; Fleischer (1908) gives 21 out of 30; Marburg (1920) 14 out of 24; Langenbeck (1914) 33 1/3 per cent.; Behr (1924) states that 70 per cent. "later" developed abnormal neurological signs compatible with disseminated sclerosis; Weill (1923) states that of 23 cases examined, 11 already had disseminated sclerosis and that a further five had developed it "some" years later; Friedinger (1925) followed up 25 cases from five to twenty years, 16 of these being followed for 11 years and two had by that time developed disseminated sclerosis—one other case was found in the other nine cases followed up for 20 years. Lactation optic neuritis described by Langenbeck (1914) and Schöppe (1919) was regarded as probably disseminated sclerosis by the former author, for a third of his cases were later found to develop this disease. Hensen (1924) states that a persisting scotoma is later associated with abnormal neurological signs.

Lenoir (1917), on the other hand, states that practically no cases developed signs indicative of a disseminated lesion. The literature on the subject is therefore conflicting, few cases having been followed for any length of time; this article is therefore concerned with the ultimate prognosis of retrobulbar neuritis followed up for over ten years.

### Investigation

The out-patients record of the Bristol Eye Hospital from 1933 to 1937 were searched for patients diagnosed as suffering from retrobulbar neuritis. Included in this unselected series are cases due to all causes except syphilis, and to them are added patients attending the in-patient department as far back as 1902. Cases were diagnosed on suddenness of onset of visual failure, papillitis in some cases and usually recovery of vision through a central scotoma. Only forty-six patients so diagnosed were found; eleven of these could not be traced due to changes in address and bombing in the war years, but four deaths which were traced are included in the remaining thirty-five of the series.

### Age of onset.

The age of onset varied from 14 to 63 years; in the untraced series the average age was 30 years and in the traced 27 years; the ratio of female to male was six to five in the untraced and nineteen to sixteen in the traced. There appeared to be no significant difference in the age of onset as regards sex in either series.

### Deaths

Four deaths were found in the series studied; one patient was killed in an accident and two died of natural causes; in none of these could death be connected with a demyelinating process. It is of particular interest that one patient who had a bilateral retrobulbar neuritis and had a negative blood Wassermann, but in whom no cerebrospinal fluid examination was made, died of general paralysis of the insane in a mental institution eight years later; it therefore appears that examination of the cerebro-spinal fluid should be carried out in cases of retrobulbar neuritis.

### Relation to pregnancy

Out of ten women examined who had had children, only two related their onset of symptoms of eye trouble to pregnancy, but one woman had later developed an acute disseminated lesion following a further pregnancy (Case 14).

### Occupation

No special incidence of any occupation was found; one patient out of the traced series had worked as a pottery glazer and he was the only one who was definitely exposed to lead.

The left eye was affected in twenty-three cases, and the right in thirteen; ten patients had bilateral involvement. Six of the latter were examined; two were found to be blind in both eyes (Cases 4 and 29), two had made a complete recovery in one eye and two had made a complete recovery in both eyes. Of the other twenty-four traced cases only one was found to be blind in the affected eye. Indeed, most patients made a complete recovery in visual acuity of the previously affected eye; the ultimate prognosis of visual acuity appears therefore to be quite favourable.

### Incidence of nervous disease in relatives

In one case only was there a familial incidence of a nervous disease (Case No. 13). This patient's sister had died three years previously to the patient's onset of retrobulbar neuritis; her hospital record notes showed that she was admitted for investigation of blindness and a "Parkinsonlike" tremor associated with bilateral extensor responses at the age of seventeen, and that she died six months later at home, no post-mortem being performed.

### Fundus

Examination of the fundus showed varying degrees of optic atrophy in the eye previously affected by optic neuritis.

### Abnormal neurological findings at the onset of ocular neuritis

Available records showed that four out of the thirty-six traced cases had abnormal findings when examined by a neurologist at the time of onset of retrobulbar neuritis; these four cases (Nos. 24, 28, 8 and 11) will now be described briefly.

CASE 24.—Fourteen years previously, when aged sixty-three years, the patient had developed an acute pain in the left eye with vision reduced to  $\frac{1}{2}/60$  and a central scotoma present on examination of the fields. At that time he had a left extensor response, but no other abnormal neurological signs; examination of the cerebrospinal fluid showed normal protein, Lange curve and cells with a negative Wassermann. On examination at follow-up, the patient's acuity was now 6/6, the left optic disc was pale and the left plantar response was still extensor; there were no other abnormal neurological findings nor had the patient had any abnormal subjective feelings in the interim period.



CASE 28.—Twelve years previously, when aged fourteen years, the patient's vision had failed suddenly with reduction of acuity to 1/60 in both eyes. X-rays of skull and sinuses were normal; blood and cerebro-spinal fluid Wassermann were all negative, and examination of the central nervous system showed the presence of bilateral extensor responses. When examined at a follow-up the patient felt quite fit and had served throughout the 1939-45 War in the Pioneer Corps. His visual acuity was now limited to perception of finger movements in the right eye, and 6/36 in the left; examination of the fundi showed a bilateral optic atrophy more advanced in the right than in the left. The rest of the central nervous system was normal except for a right extensor response. He, too, had no subjective evidence of any abnormal neurological disorder.

CASE 8.—This patient, an agricultural labourer, developed an acute failure of vision seventeen years ago when aged thirty-two years; at that time he had bilateral blurring of the optic discs with acuity reduced to 4/60 in the left and 6/36 in the right, the cerebro-spinal fluid examination was normal in all respects, except for the Lange curve of 12222100; his plantar responses were extensor. When examined at follow-up, he had a bilateral optic pallor, visual acuity 6/9 right and left, and no abnormal neurological signs except for bilateral extensor responses. He felt well and was actively employed as a farm tractor driver.

CASE 11.—This patient developed a sudden blindness of the right eye twenty years ago when aged eighteen years. At that time she had a papillitis of the right optic nerve and bilateral extensor responses. Since then she had gradually developed further neurological lesions year after year, with intermissions and exacerbations. On follow-up examination she was bed-ridden, with bilateral optic atrophy, nystagmus in all directions, paresis of the left sixth cranial nerve and a gross inco-ordination of arms and legs. She had a severe degree of impairment of joint sensibility, worse in the legs than the arms, and a spastic quadriplegia with bilateral extensor responses completed a depressing picture.

The presence of abnormal neurological findings in a patient with a retrobulbar neuritis does not necessarily indicate a bad prognosis, as the above case records show that some patients lead full and active lives for many years afterwards.

#### **Incidence of further abnormal neurological findings compatible with the diagnosis of a demyelinating disease**

Abnormal neurological findings were present in twelve of the thirty patients examined: six of these could be definitely diagnosed as suffering from disseminated sclerosis, and six probably affected

TABLE I

Years followed up	Number of cases	Number with definite Disseminated (Case series numbers in brackets)	Number with probable Disseminated (Case series numbers in brackets)	Number with no evidence of Disseminated (Case series numbers in brackets)
10	1	0	0	1 (20)
11	2	0	0	2 (12.31†)
12	4	2 (2.3)	1 (28*)	1 (30)
13	7	0	1 (6)	6 (10.15.16.17.18.25)
14	10	3 (5.14.21)	1 (24*)	6 (1.9.12.22.26.27)
17	1	0	1 (8*)	0
19	1	0	0	1 (23)
20	2	1 (11*)	1 (7)	0
45	2	0	1 (4)	1 (29)
47	1	0	0	1 (19)
Total	31	6	6	19

\* = Had abnormal neurological findings at onset of retrobulbar neuritis.

† = Refused to be examined.

by this disease. The findings varied greatly, some had numbness of both legs, others transient numbness of leg or arm, and others said they were quite well but on examination abnormal plantar responses were found. One only of the whole series (Case 11) was confined to bed, all the rest were in fact leading useful and productive lives, for the two blind patients were employed at basket making.

### Discussion and Summary

The purpose of this paper was to discover how many patients with retrobulbar neuritis eventually developed disseminated sclerosis after a number of years. Only five patients answered a written questionnaire by post, stating that they had nervous diseases, but in fact twelve out of thirty cases actually examined showed evidence of abnormal neurological findings. The incidence of previous organic disease amongst the population is therefore probably much higher than is usually realised, for only three of these twelve patients were under medical supervision and only one of these was bed-ridden. This may indicate that the occurrence of disseminated sclerosis is higher than previous figures have shown.

The prognosis for visual recovery appears to be excellent on the whole, only one out of the twenty-five unilateral cases being blind in the affected eye a considerable number of years after. The prognosis with regard to further demyelination elsewhere in the central nervous system is more difficult to estimate; in fact it is impossible to give a prognosis in these cases, as one patient with a bilateral retrobulbar neuritis was in excellent health forty-seven years later. In addition, it has been shown in this survey that the presence of abnormal neurological findings at the onset of retrobulbar neuritis does not necessarily mean a bad prognosis.

The eleven patients who were untraced might conceivably have died of disseminated sclerosis, but it is suggested that migration of population during the war years had a great deal to do with the fact that they were untraceable. In fact, three of these were domestic servants and one was an inmate at a Salvation Army Hostel.

Finally, the importance of doing not only blood Wassermann reactions on these patients but full cerebro-spinal fluid examinations to exclude syphilis is stressed in this paper. One patient in whom this was neglected was later found to have developed cerebral syphilis.

### Conclusions

1. Forty-six cases of retrobulbar neuritis were taken from hospital records. Eleven were not traced, four were dead and one

refused examination. The thirty cases left were examined from ten to forty-seven years later.

2. Twelve patients were found to have abnormal neurological signs apart from the eyes, but only one was bed-ridden with disseminated sclerosis.

3. The eventual prognosis of visual recovery was good. Of the twenty-four unilateral cases, one was blind; and of the six bilateral cases two were blind in both eyes and two blind in one eye.

4. The importance of examination of cerebro-spinal fluid for evidence of syphilis in cases of retrobulbar neuritis is stressed.

I wish to thank Dr. A. M. G. Campbell for his continued interest and help in the compilation of this work, and the Honorary Staff of the Bristol Eye Hospital for allowing me to see their case notes.

### Case histories

#### A. DEFINITE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 2. Female. Sudden onset of painful blindness of left eye with papillitis twelve years ago when aged twenty-one. Seven years ago the patient developed transient numbness below the umbilicus, which recovered; since then had further attacks of numbness. On examination there was loss of vibration sense and joint sense in the left arm and right leg. The diagnosis of disseminated sclerosis had been confirmed by Professor Cloake, of Birmingham.

CASE 3. Female. Sudden onset of painful blindness in right eye twelve years ago, when aged twenty-six. Complete recovery of vision in a month followed by a recurrence in the same eye nine years later with an associated numbness up to the middle of the waist. Examination now showed loss of vibration sense in the left leg with bilateral extensor responses.

CASE 5. Female. Sudden onset of loss of vision in the left eye when aged twenty-seven, fourteen years ago. Recurrent ataxic episodes since, transient numbness in face and left arm with peripheral numbness recently. Diagnosed as disseminated sclerosis by Dr. Russell Brain.

CASE 14. Female. Sudden failure of right vision fourteen years ago, when aged twenty-one. The patient had been quite well till nine months prior to examination when, following a pregnancy, she developed subjective numbness from the umbilicus downwards. Physical examination revealed a sensory loss below the level of the eighth thoracic dermatome, and a spastic paraplegia with bilateral extensor responses.

CASE 21. Female. Sudden onset of failure of left vision fourteen years ago, when aged twenty-two. The patient stated she felt quite well, but physical examination showed ataxia and diminished vibration sense in the left leg, with bilateral extensor responses.

#### B. PROBABLE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 4. Male. Sudden failure of vision of the right eye forty-five years previously, when aged sixteen. This recovered after a few months, but two years later he developed a visual failure of the left eye; this too recovered. At the age of thirty-three the patient developed blindness in his right eye from which he never recovered, and at forty-two he developed a blindness of the left eye. On examination at the age of sixty-three, the patient was completely blind in both eyes with a bilateral optic atrophy; he had bilateral extensor responses but made

no complaint of any ill-health at all and was actively employed at basket-making.

CASE 6. Male. Sudden onset of painful visual failure in left eye when aged thirty-five, twelve years ago. Complete recovery of visual acuity. Patient stated he felt quite well (a patient in Hain Green Sanatorium for pulmonary tuberculosis), but bilateral extensor responses were found on examination.

CASE 7. Female. Sudden onset of failure of vision in the right eye twenty years ago, when aged twenty-three. Patient had developed numbness in the right leg 14 days prior to examination; this was confirmed by sensory testing, and there was found to be a right extensor response.

### C. NO EVIDENCE OF DISSEMINATED SCLEROSIS.

CASE 1. Male. Sudden onset of painful blindness of left eye with papillitis fourteen years ago, when aged twenty-five. No abnormal neurological signs now.

CASE 9. Male. Sudden onset of visual failure in the left eye fourteen years ago, when aged twenty-two. No abnormal neurological findings now, and no subjective symptoms.

CASE 10. Male. Sudden onset of right visual failure associated with pain fourteen years ago, when aged twenty-one. No abnormal neurological findings now, and no subjective symptoms.

CASE 12. Male. Sudden onset of left visual failure eleven years ago, when aged thirty-six. Since then there have been no symptoms of neurological disease.

CASE 13. Female. Sudden failure of left vision fourteen years ago, when aged twenty-three. Since then there have been no symptoms of neurological disease.

CASE 15. Female. Sudden failure of left vision thirteen years ago, when aged thirty-four. Since then there have been no symptoms of neurological disease.

CASE 16. Female. Sudden failure of left vision thirteen years ago, when aged fifty-two. Since then there have been no symptoms of neurological disease.

CASE 17. Female. Sudden failure of left vision thirteen years ago, when aged twenty-two. Since then there have been no symptoms of neurological disease.

CASE 18. Male. Sudden failure of right vision thirteen years ago, when aged twenty-one. Since then there have been no symptoms of neurological disease.

CASE 19. Female. Gradual failure in vision in both eyes in a few days without pain associated with a bilateral papillitis forty-seven years ago when aged twenty-one years. Visual acuity in the left eye 6/12, but hand movements only are perceived in the right eye. Since then there have been no symptoms of neurological disease.

CASE 20. Male. Sudden onset of visual failure ten years ago, when aged forty years. Since then there have been no symptoms of neurological disease.

CASE 22. Female. Sudden onset of left visual failure fourteen years ago, when aged thirty-two. Since then there have been no symptoms of neurological disease.

CASE 23. Female. Sudden onset of left visual failure nineteen years ago, when aged twenty-eight. Since then there have been no symptoms of neurological disease.

CASE 25. Female. Sudden onset of bilateral painful failure of vision with papillitis thirteen years ago, when aged twenty-four. Visual acuity now 6/6 right and left. Since then there have been no symptoms of neurological disease.

CASE 26. Female. Sudden onset of left visual failure when aged thirty-eight years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 27. Male. Sudden onset of left visual failure when aged eighteen years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 29. Female. Sudden bilateral failure of vision forty-five years ago, when aged seventeen. Partial recovery for nine months afterwards, and then a relapse into complete and total blindness. Examination showed a bilateral primary optic atrophy but no subjective or objective evidence of disseminated sclerosis.

CASE 30. Male. Sudden onset of right visual failure eleven years ago, when

aged twenty-nine. Since then there have been no symptoms of neurological disease.

CASE 31. Female. Sudden onset of left visual failure eleven years ago, when aged twenty-six. Patient refused to be examined and said she was quite well.

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## TREATMENT OF SEVERE INFECTED CORNEAL ULCERS BY SUBCONJUNCTIVAL INJECTIONS OF PENICILLIN TWICE DAILY WITHOUT HOSPITALIZATION, WITH SHORT REVIEW OF OTHER METHODS\*

BY

KAMEL RIZK

EL-MINIA, UPPER EGYPT

OCULISTS, like myself, who work alone in their clinics without medical assistants, look for a method of penicillin administration, which is practical, efficient and economic for the successful treatment of infected corneal ulcers. By the word "practical" I mean that it should not cause much strain either to the doctor or to the patient, or to his attendants at home, and should not interfere with their sleep. By the word "efficient" I mean that it should be able to control the infection instantly so that it spreads no more, and this control must be followed by rapid improvement and progressive healing. By the word "economic" I mean that the method should

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not imply the use of much penicillin, as some patients are unable to pay the cost of penicillin if massive doses are to be used daily for few days. This point assumes special importance when we notice that severe infected ulcers of the cornea in Egypt mostly occur in the poorer classes who do not seek for medical advice except when their condition is very bad.

A brief review of the chief methods used is necessary, and we have to consider them in the light of the three criteria mentioned above.

One of the methods of penicillin administration for ocular affections is the systemic mode of administration used for a great variety of infections in general medical practice. Penicillin need not be administered intra-muscularly in aqueous solution or saline every three hours as this is not practical, but it can be given in massive doses suspended in oil and beeswax twice daily.

Sorsby and Ungar (1946a) showed that penicillin administered systemically in massive doses reaches in therapeutic levels all the tissues of the globe, the lens excepted. By massive doses is meant the injection of 25,000 to 50,000 units intra-muscularly or intravenously into rabbits of an average weight of 1.5 kilograms. Duke-Elder (1947) commenting on this fact says that this dose is of the order of 40 or 50 times that of the usual clinical dose in man. We can imagine that massive doses administered systemically for ocular purposes must be very expensive apart from the other disadvantages such as difficulty of administration.

Local therapy by subconjunctival injections is much more economic than massive therapy by systemic administration. It may be noted that whenever subconjunctival injections of penicillin are mentioned in this paper only the pure crystalline white calcium or sodium salt is meant because it is well tolerated. Sorsby and Ungar (1947) showed that substantial concentrations of penicillin in the ocular tissues many times the usual therapeutic level can be obtained by the subconjunctival injection of crystalline penicillin in a dose of 50,000 units and that adequate levels persist for 6 hours. Sorsby and Reed (1947) subsequently elaborated their method of local penicillin therapy in cases of hypopyon formation by 12 to 16 subconjunctival injections of 50,000 units every 6 hours, followed by the 4 hourly instillation of penicillin ointment in a concentration of 100,000 units per gram. Among their group of 66 cases with hypopyon, there were 39 cases of infected corneal ulcers.

These authors made a detailed analysis of these cases of infected corneal ulcers with hypopyon treated by different methods of local penicillin therapy. They show subconjunctival injections to be the method of choice. It was successful in 18 out of 21 cases so treated. In three patients subconjunctival injections of penicillin proved inadequate and general sulphonamide therapy was applied. This

method of penicillin therapy by subconjunctival injections every six hours cannot be applied except in hospitals with resident doctors who can give the injections by night. Moreover as it entails the use of 200,000 units per day, it cannot be said to be economic. But there is no doubt that it is the most efficient method.

For general penicillin therapy the use of penicillin in oil and beeswax has greatly reduced the number of injections so that two injections can be given daily. The question, as to whether the same material can be used subconjunctivally twice daily, arises. Sorsby and Ungar (1946b) found by animal experiments that such a procedure gave a high and sustained level of penicillin, but it was clinically inapplicable in ocular affections as it produces a severe reaction with gross corneal damage.

It was by chance that I was forced to try the use of two injections of penicillin daily. During the summer of 1947, a shortage of the supply of penicillin occurred in Egypt, and it was very difficult to get it except for few patients after complicated procedures. Under such a condition, extreme economy in the use of penicillin was necessary. The first case in which subconjunctival injections of penicillin were used by me is worth being reported in detail as it impressed upon me the efficiency of subconjunctival injections twice daily, as well as its superiority over some other methods of local penicillin therapy.

#### Case Report with Comment.

On 18th July, 1947, M.S., a male rural infant, aged 18 months, was brought to my clinic by his parents. There was a history of typhoid fever of one month duration, towards the end of which he became very thin and developed an opacity in the right eye since four days ago and in the left eye since two days ago. On examination, he was found to be very emaciated, but there was no fever, and apart from his eyes, there was no other abnormality. The right conjunctiva was injected. There was a large deep ulcer in the right cornea, which occupied almost all the lower half of the right cornea and encroached on the upper half, covering the whole pupillary area. Its base was dirty, sloughing and thin and there was a severe hypopyon occupying about one quarter of the anterior chamber. The left conjunctiva was injected. There was an ulcer in the lower part of the left cornea occupying about one sixth of the corneal surface. No hypopyon existed in the left eye.

General treatment by the appropriate diet, vitamins and tonics was carried out by a paediatrician.

It was evident that the right eye was in a most serious state and there was a great danger of its being lost. In an attempt to save the right eye, I decided to use penicillin in this case, and to use it



economically as there was a great shortage of this drug at that time. An amount of 10 c.c. of distilled water was put in a bottle of 100,000 units of crystalline penicillin; 3 c.c. of the solution were taken, and diluted with 9 c.c. of distilled water so that a solution containing 2,500 units per c.c. was obtained, and this was used as drops for both eyes after a preliminary wash of the eye. The treatment started at about 10 a.m., and consisted of the instillation of two drops of that solution in each eye every minute for the first half-an-hour, then every five minutes for the next half-an-hour. At the end of the first hour, the left ulcer improved, and its base became clearer. The improvement in the right ulcer was dramatic. Its base which was very dirty, became clearer to a marvellous extent. The application of drops for the first hour was carried out by the nurse, but after this first hour, I sent the patient home with instructions to his parents to instil the drops every half-an-hour. At 7 p.m., I saw the patient again and the condition of both ulcers was as bad as when first seen. The parents denied any neglect, but probably there was gross neglect, as the type of parents, who bring their child to medical treatment only when the disease is far advanced, are usually negligent. It is equally possible that in this case half-hourly instillations of penicillin drops were not adequate. Again I repeated the instillations just as in the morning, every minute for the first half-an-hour, then every five minutes for the next half-an-hour. Again the same marvellous improvement occurred, and again I sent the patient home with instructions to use drops every half-an-hour as long as either of his parents could keep awake by night, noting that penicillin in oil and beeswax for systemic administration was not available. Next morning both eyes were seen to be as bad as when first seen. It seemed that though the case responded well to penicillin, some change in the mode of administration must be made. Probably half-hourly instillations at home were not adequate but more frequent instillations were very tedious to the attendants and did not seem to be practical. Probably some neglect in following the instructions was responsible for the failure. Subconjunctival injections seemed to offer a mode of treatment which the attendants could not affect by their neglect. These had to be carried out twice daily, as I could not give them more frequently with convenience. 0.5 c.c. of the solution already prepared in the bottle was injected twice daily in each eye. This amount contained 5,000 units of penicillin. Seven subconjunctival injections were given in each eye over a period of three and a half days. Rapid and progressive improvement was noticed during this short course. Apart from atropine ointment twice daily no other treatment was applied locally.

Towards the end of the course the base of each ulcer was quite clear and the right hypopyon disappeared. Owing to the shortage of penicillin no more injections could be given. Lamellae of penicillin,

each of 250 units, and penicillin ointment of a concentration of 1,000 units per gram were prescribed and were ordered for use every hour alternately. They were used during daytime and most of the night, and the application was made by the mother at home. Twenty-four hours from the onset of the use of lamellae and ointment, the base of the ulcers on both sides became gray and infiltrated.

This indicated that penicillin injections should be resumed, but no crystalline penicillin was available for further injections. Two days later the right ulcer perforated with the formation of a small prolapse of iris. Rapid healing of the right ulcer followed the occurrence of the iris prolapse. Healing of the left ulcer occurred without prolapse.

The behaviour of the right ulcer seemed to show that lamellae and ointments of the concentration mentioned above are not so efficient as subconjunctival injections. Moreover the difficulty of their application safely in infants and young children, who often struggle during their application, renders their use at home unsafe in cases of ulcers with thin base because of the danger of inducing perforation. Also the possibility of neglect exists with such types of patients.

#### Further Development and Details of the Method of Subconjunctival Injection of Penicillin Twice Daily

The case mentioned above pointed to a method of penicillin administration which was practical, efficient and economic. It was worthy of further trials and attempts towards perfection.

Patients dislike subconjunctival injections and the majority object to them. Two instillations of 1 per cent. pantocaine solution at three minutes intervals while the eyes are closed are harmless to the epithelium and produce sufficient anaesthesia to allow the prick of the needle to be done almost painlessly.

Apart from the prick of the needle, the mere infiltration of fluid under the conjunctiva causes some pain while the fluid is actually passing and for some time afterwards and this pain can be easily abolished if 1 per cent. novocaine solution in non-pyrogenic distilled water is used instead of simple distilled water in the preparation of penicillin solution.

A concentration of 20,000 units per c.c. was found to be quite satisfactory in cases where 10,000 units per c.c. was not quite satisfactory. Therefore to a bottle of 100,000 units of crystalline penicillin salt, 5 c.c. of 1 per cent. novocaine solution in distilled non-pyrogenic water was added, and 0.5 c.c. was injected subconjunctivally twice daily, at about 9 a.m. and 8 p.m., each injection being given after two instillations of 1 per cent. pantocaine solution. The eye is opened and partially fixed by a pair of Desmarres' retractors applied to the lids with their tips introduced into the fornices if the patient is unable to open and fix his eye while the injection is being given subconjunctivally at a distance of 2 to 3 mms. from the limbus.

The use of Desmarres' retractors is specially valuable when the injection is given above the limbus. It is advisable to change the site of injection every time. Even in unsteady nervous children, the injections can be safely given. The trunk and hands are fixed by another nurse; the nurse holding Desmarres' retractors assists slightly in fixing the head by the same hands; and the doctor can use one hand for fixing the head while the other hand holds the syringe and gives the injection.

One bottle of 100,000 units is enough for a course of 5 days which is usually sufficient. The addition of adrenalin chloride solution to penicillin solution to render it less readily absorbable into the general circulation is liable to destroy the penicillin especially because of the long period of 5 days over which the acid adrenalin chloride acts on penicillin while it is in the bottle until it is completely exhausted. The destructive effect of solutions, even of poor acidity on penicillin was demonstrated by Garrod (1945). Therefore no adrenalin chloride solution, which is acid, may be added to penicillin solution (Cameron 1945).

One course of 10 injections is usually sufficient for almost all cases. At the end of the course the healing of the ulcer is progressing well, and it is quite sufficient to use frequent wash and hot fomentations after stopping the injections. If the slightest sign of infiltration recurs, the course may be repeated partially or completely according to the discretion of the oculist.

In addition to penicillin injections, atropine ointment 1 per cent. twice daily is applied as a routine in all cases, except in eyes predisposed to glaucoma.

No other local or general treatment was applied in the majority of cases as long as the injections were given. But frequent wash and hot fomentations were used after the course was completed.

In a small proportion of cases, the improvement produced by the first few injections was slight. In them the use of frequent wash, hot fomentations and local sulphadiazine ointment 5 per cent. every two hours, in addition to subconjunctival injections of penicillin, helped to accelerate cure.

It may be noted that in general medical practice some practitioners dislike the use of penicillin in oil and beeswax, and use massive doses of penicillin in water two or three times daily with good clinical results. The success of subconjunctival injections twice daily runs parallel with the success of massive doses of aqueous solutions of penicillin administered twice or thrice daily in general medical practice.

If there is muco-purulent or purulent discharge in the conjunctival sac in cases of corneal ulcers, subconjunctival injections of penicillin should not be administered before the discharge is controlled by

penicillin drops in the mode suggested by Sorsby for ophthalmia neonatorum. A solution of crystalline penicillin of a concentration of 2,500 units per c.c. is prepared. Two drops are instilled into the eye every minute for the first half-an-hour, then every five minutes for the next half-an-hour. At the end of half-an-hour, the discharge practically ceases in penicillin sensitive cases, but the drops should be continued every five minutes for another half-an-hour. Then subconjunctival injections can be started. If the discharge is resistant to penicillin drops, subconjunctival injections are contraindicated for obvious reasons. The micro-organism causing the ulcer is that of the associated conjunctivitis and as the discharge causing the conjunctivitis is not controlled by penicillin, the micro-organism is penicillin resistant and no useful purpose is served by subconjunctival injections. Moreover there is obvious danger of deep infection in the orbit. Fortunately, cases of conjunctivitis with severe ulcers of cornea are usually sensitive to penicillin.

### Comparative Value of this Method

No attempt is made to compare the therapeutic value of the method of subconjunctival injections of penicillin twice daily with the method of subconjunctival injections every six hours. The practical disadvantages of the latter method have already been mentioned.

A comparison between this method of two subconjunctival injections of penicillin daily as detailed above and the routine older methods of treatment without penicillin is to be considered.

In pre-sulphonamide days the routine treatment of infected corneal ulcers was by frequent wash, hot fomentations and atropine ointment. To these, foreign protein therapy was very frequently added. Milk injections are the form in which foreign protein is usually administered in Egypt. Ten c.c. of sterile milk are administered intra-muscularly every other day. A course of 2 to 5 injections is usually given. Milk injections usually cause rapid clearing of infected corneal ulcers, but very frequently ulcers grow much deeper and even perforate while milk injections are administered, and ophthalmologists in Egypt believe that this increase in depth, and even perforation, are provoked by milk injections.

General sulphonamide therapy formed a substitute for milk injections and was used in addition to frequent wash, hot applications and atropine ointment. Sulphathiazole was administered in doses of one gram. four or five times daily. This treatment could not control the progress of the ulcer for 2 or 3 days or even more. Severe ulcers frequently perforated in spite of this treatment.

Penicillin therapy, in the method detailed above, has the great value of immediately controlling and stopping the progress of the

ulcer from the first injection. Then the base and margins of the ulcer quickly get progressively clearer, and gradually healing occurs. Only severe infected ulcers of the cornea were selected for this form of therapy. Milder forms of corneal ulceration were excluded as they responded rapidly to older methods of treatment. The severe cases selected for penicillin therapy were 26 in number. Some of them were traumatic with or without hypopyon but most were secondary to purulent conjunctivitis and a few were secondary to mucopurulent conjunctivitis. Most of them responded rapidly, almost immediately to subconjunctival injections of penicillin as detailed above. The progress of the ulcers was stopped after the first injection; then the base and margins became clearer and progressive healing followed.

Few cases showed slight response and the improvement produced by the first few injections was slight. In them penicillin can be said to be inadequate and the use of frequent wash, hot fomentations and local sulphadiazine ointment 5 per cent. every two hours during daytime, in addition to subconjunctival injections of penicillin helped to accelerate cure. Not a single case of perforation occurred in this series of 26 cases of severe infected corneal ulcers.

### Conclusions

This method of treatment yields better results than the older methods of treatment in which general sulphonamide therapy or foreign protein therapy formed a part of the treatment. This claim is supported by general clinical observation as mentioned above, but no comparative statistics were made. This method is considered to be a practical, efficient and economic mode of penicillin administration in severe infected corneal ulcers.

### Summary

A method of treatment of severe infected corneal ulcers by subconjunctival injections of penicillin twice daily is described.

The value of this method compared with the older methods of treatment is discussed. This value is demonstrated by general clinical observation but no statistics were made.

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OPERATION FOR PERSISTENT PUPILLARY  
MEMBRANE. NOTES ON A CASE\*†

BY

ZOLTÁN BÁTHORI

BUDAPEST

SINCE the use of the slit-lamp the diagnosis of persistent pupillary membrane has become very frequent, and even the smallest vestige of the condition can easily be recognised. It may appear in a variety of forms and though the condition is frequent (according to Staehli 31 per cent. of all cases) it is extremely rarely that it interferes with the patient's vision, or that an operation has to be done to improve sight.

The first operated cases were published by Wiegmann (1916). He operated on four eyes of a pair of twins, and after several repeated operations the vision improved. Mawas and Terrien (1922) refer to a histological examination of a persistent pupillary membrane which was removed by operation and in this case too vision had improved. In a case of Noji (1930) optical iridectomy was performed as the persistent pupillary membrane was adherent to the lens capsule and partial lenticular opacities were present. A good result was achieved. Nakame (1937) refers to several operated cases. It is interesting that in spite of the number of reported cases text-books of ophthalmology, or of operative eye surgery do not describe an operation for the condition.

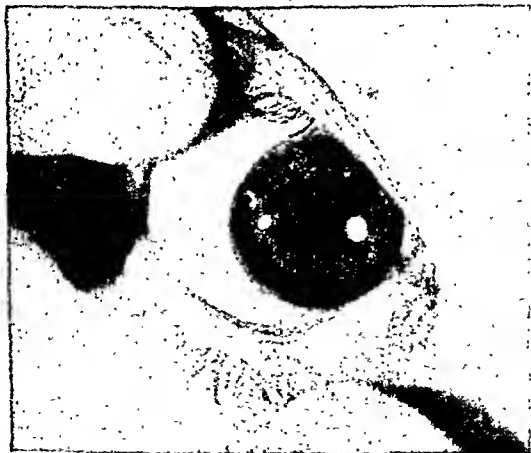


FIG. 1.

\* From The Eye Clinic of Pázmány Péter University, Budapest,  
(Director: Prof. Joseph Imre.)

† Received for publication, January 27, 1948.

In 1934 I presented a patient to the Hungarian Ophthalmological Society with a dense persistent pupillary membrane occupying the whole area of the pupil (Fig. 1.).

30 years old woman, had always poor vision. She noticed recently further deterioration. V.A. R.E. Counting Fingers 3m. — 3'0 D.sph. 5/50.

L.E. 5/30 — 3'5 D.sph. 5/12.

Nystagmus of small amplitude, mainly in the horizontal direction.

R.E. The pupillary area was occupied by a mass of brownish tissue, identical in colour with the iris, slightly prominent. With the slit-lamp it showed a dense central part of 1.5mm. diameter, and from here a mesh of threads of different thickness originated, passing in radial direction towards the iris crypts. The pupillary margin could be seen through the mesh, and the pupil was active. The lens appeared clear.

L.E. showed a similar but less marked picture. The central dense mass was of only 0.5mm. diameter. Lens, media and fundus showed no abnormal changes.

Operation on the right eye was performed by Professor Imre.

After a keratome incision the filaments were pulled into the wound, one by one, with a small iris hook and severed with de Wecker's scissors, and eventually the whole persistent pupillary membrane was removed. After operation the whole area of the pupil was clear

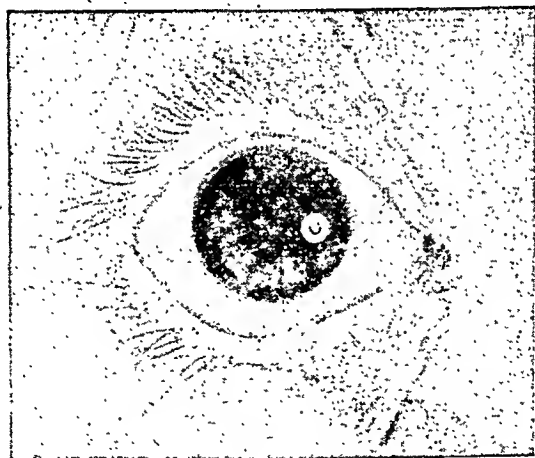


FIG. 2.

(Fig. 2.) and vision had improved with glasses to 5/8. The left eye was not operated upon.

We think that in cases where the vision is reduced by persistent pupillary membrane an operation is indicated, and the operation of choice is:

- (1) as above described, if the persistent pupillary membrane is free and not adherent to the lens capsule, or
- (2) an optical iridectomy if it is adherent to the lens capsule.

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ANNOTATION

Dislocated Lenses

The lens may be dislocated either forwards or backwards by direct or indirect violence. We remember a case in the latter category in a patient of many years standing. On his first visit he was wearing a medium myopic correction with the stronger glass in the right side. He had a cataract in this eye, the other lens being clear and vision corrected to 6/6 and J.1. The right eye had perception and projection of light and as far as we could see there were no keratic precipitates. This patient visited us for about twenty years at regular intervals. On no occasion could we see any precipitates, but we could never feel quite sure that the condition had not arisen in consequence of some low grade inflammation: and as he was used to his restricted field of vision and had good vision in the other eye we refused to suggest an operation.

This patient about eighteen months before his death had a slight accident. He slipped on his own doorstep and sat down rather heavily. Soon after, he called to say that he could see more light than usual in his bad eye. The upper margin of his lens was visible in the upper part of his pupil and by degrees the lens vanished into the bottom of his eye and vision of 6/18 could be obtained with a suitable lens; but he was not happy and preferred to wear a black patch on the right side. When he died, in his 80th year, the lens was still in the depths of his eye.

On only one occasion were we called upon to deal with a lens dislocated into the anterior chamber. This was in an old man who had been an out-patient for many years. He was a marked case of interstitial keratitis and his left cornea was so much scarred and flattened that the eye was useless. The right eye had very poor vision, not more than hand movements. The family had been celebrating Christmas and the two sons became quarrelsome. In trying to separate them the patient received a heavy blow with a fist in his right eye and the lens was dislocated into the anterior chamber. We dealt with it in the usual way under a general anaesthetic. A needle was passed into the dislocated lens from the limbal area, to fix the lens and given to the house-surgeon to hold, a keratome section was made and the lens extracted with a vectis. He left hospital with perception of light and we did not see much more of him.



## OXFORD OPHTHALMOLOGICAL CONGRESS 1948.

THE 34th annual meeting of the Oxford Ophthalmological Congress was held on July 8th., 9th. and 10th. The increasing popularity of this conference necessitated a change of venue, and this year the congress was housed in Hertford College, while the proceedings were conducted in the School of Geography since the theatre of the School of Human Anatomy could no longer offer sufficient accommodation.

The Master, Mr. F. A. Williamson-Noble, opened the congress on Thursday morning with an address of welcome. After this Dr. Arthur Greene made a presentation to Dr. F. A. Anderson, on his retirement as secretary of the congress, of a cheque subscribed by members in token of their appreciation of his untiring efforts and notable success in forwarding the interests of the congress for the past 12 years. Dr. Anderson expressed his thanks and the pleasure he had derived from his work as secretary.

The subject for discussion, "the use and abuse of topical ocular therapy," was opened by papers by Mr. F. Ridley, Dr. F. E. Preston and Dr. J. M. Robson. Mr. Ridley drew attention to the tear-film and described its anatomical position and physical properties. He emphasised that lysozyme normally kills all airborne bacteria and also the common pathogenic organisms, and that it is destroyed or inhibited by drugs containing free halogens and by acriflavine. The lysozyme content is reduced in interstitial and phlyctenular keratitis, and is increased by the use of atropine in these diseases, and a return to a high level presages the recovery of the patient. In the use of drugs in the conjunctival sac dilution occurs rapidly, and few drugs retain an effective concentration for long. Solutions are diluted by half every 45 seconds, but emulsions are retained longer. The latter should, when possible, be emulsion of oil in water, not the reverse, and thereby an increased corneal permeability is obtained. With reference to atropine irritation the approximate ratios of solutions, lamellae and serum of atropine and hyoscine were indicated, showing that lamellae hyoscine were eight times less irritant than solution of atropine. Mr. Ridley considered that irritation could almost invariably be avoided by the use of lamellae. Local sensitisation was due to the presence of histamine-like bodies in the tears, which are neutralised by the normal aqueous, but this mechanism is defective in certain diseases.

Dr. Preston considered ocular therapy as of two schools, the empirical and the rational. He noted that the secondary effects of drugs may sometimes prove more valuable than those of their original purpose. He then gave a number of specific instances of valuable applications in particular conditions.

Dr. J. M. Robson spoke of the value of local application in obtaining a higher concentration than could safely be reached by systemic therapy. The limiting factor in the value of many drugs was the rapidity of local elimination. He mentioned four methods of overcoming this difficulty by (1) iontophoresis, (2) deturgescent agents, (3) subconjunctival injection, (4) intra-vitreous injection. He considered that deturgescence of the cornea had been neglected clinically, and remarked that subconjunctival injection should be combined with vaso-constriction.

In the subsequent discussion the influence of allergy was referred to by Dr. Vera Walker, the value of powders by Dr. Traquair, injection into the anterior chamber by Dr. Huber, and the abuse of penicillin by Mr. J. P. F. Lloyd.

In the afternoon, Dr. J. J. Healy read a paper on "unusual ocular injuries," and members contributed a number of equally surprising experiences.

After this, Dr. Grant Peterkin contributed an interesting paper on "dermatological conditions affecting the ocular adnexa." He divided the conditions under review into (a) new growths, (b) oedematous swellings of the lids, (c) Tuberculosis cutis and allied diseases, (d) Systemic diseases; his descriptions were accompanied by numerous coloured illustrations. He laid stress on the frequency of contact dermatitis in many obscure cases of lid swelling and mentioned the characteristic features. His experience with acne rosacea had been variable and often disappointing. He had noted much dermatitis from the superficial application of sulphonamide and penicillin ointments and creams.

Mr. Dickson Wright then read a paper on the "approach to orbital tumours" in which he advocated a wide exposure from the lateral side with temporary removal of up to  $\frac{1}{3}$  of the orbital margin. This was replaced at the end of the operation and always took well with no tendency to absorption. A film was shown of the operative technique in two cases. Mr. H. B. Stallard also showed a film of the Kronlein operation and Mr. J. Foster gave the results of his own experiences with such cases.

On Friday, Mr. F. W. Law reported an unusual "case of retinoblastoma" in which the following points were notable, (1) The involvement of the second eye while under observation. (2) The apparent total destruction of the focus in this eye by diathermy. (3) Death by distant metastasis, though both optic nerves were apparently normal during life.

Mr. F. Ridley then gave a paper on "contact lenses" and dealt with recent developments in theory and practice. Improved methods of moulding were described and also a simplified method for accurate estimation of the curvatures required for correction. Veiling, caused

by the development of negative pressure and swelling of unsupported tissues by the action of lid pressure, could be relieved by the inclusion of channels at the lower end of the lens leading into the tear pool in the lower fornix. Photophobia, closely related to veiling, was more difficult to deal with, but tinted glasses would often help.

Dr. Z. A. Leitner described the value of Grenz rays in ophthalmology. Having only minimal penetrating power they were specially safe for the treatment of superficial lesions; 98 per cent. of the rays are absorbed before reaching the lens. Success has been obtained in the treatment of corneal ulcer, recurrent erosion, superficial punctate keratitis, and phlyctenular keratitis. Mooren's ulcer did not respond to Grenz ray therapy, and acne rosacea keratitis in some cases only.

The Doyne Memorial Lecture, delivered by Sir Stewart Duke-Elder under the title of "The Blood-aqueous barrier," described the latest work on the problem of the intra-ocular fluid. By the use of neutrons tracer elements could be added to substances and, by their radio-activity, their course after intravenous injection could be followed in the ocular tissues, and much less disturbance from the normal was possible in the animals used. The presence of  $\beta$  particles in the aqueous was the basis of the examinations. From these experiments it appeared that water is derived by simple diffusion at a rate of 50 cu. ml. per minute and that the mechanism in Schlemm's canal is one of bulk flow. Water diffusion into the vitreous is  $1/5$  the rate into the anterior chamber. Sugars reach the anterior chamber by simple diffusion, but the lower ratio in the vitreous argues an additional chemical barrier to this tissue. Experiments showed that sugar is metabolised in the eye chiefly by the lens and the retina. Nitrogenous substances did not enter the aqueous so well and also were affected by the vitreous barrier, while electrolytes, with the exception of phosphate, gave similar values to sugars. Sodium, potassium and chloride reach the posterior part of the eye solely through the ciliary body and pass the vitreous barrier slower than sugars *vis-a-vis* their molecular size.

The lecturer postulated a variation of the mechanism of transference in different parts of the eye. These recent experiments lead the lecturer to the conclusion that the capillary cells, not the inter-spaces, constitute the sole barrier and that these cells show variations in selective porosity. There seems however to be evidence that the ciliary epithelium in addition actively engages in the secretion of sodium chloride.

At the conclusion the Master presented Sir Stewart Duke-Elder with the Doyne Medal.

A discussion on the "operative treatment of glaucoma" was opened by Mr. Williamson-Noble and Mr. Maurice Whiting. The

Master revealed a catholic variety of choice with a preference for iridectomy or iris inclusion in acute congestive, and cyclodialysis or iris inclusion in non-congestive cases: for buphthalmos he commended goniotomy. In association with aphakia he had found trephining less disappointing than cyclodialysis, and thought a small flap sclerotomy worthy of trial in thrombotic glaucoma. He also gave a number of practical suggestions for pre- and post-operative treatment.

Mr. Whiting reviewed the indications for operation in chronic cases. He preferred trephining for most cases in spite of admitted drawbacks, with a preference of Herbert's sclerotomy as an alternative.

Dr. F. A. Anderson mentioned the value of intravenous sucrose injections as a pre-operative measure, and described the technique of iris inclusion without introducing instruments intra-ocularly.

Dr. Traquair described his pilgrimage from trephining to cyclodialysis, thence to cyclodiathermy, and his final return to the trephine as the operation of choice.

Mr. E. G. Mackie was a frank advocate of iris inclusion and gave comparative figures of his results showing a high proportion of success.

Mr. A. G. Palin on the other hand favoured the trephine.

Mr. A. MacRae had come to prefer the modified iris inclusion operation described by Greenwood and Eggers, and gave illustrations of the technique together with a table of results.

Many other members took part in a free discussion which continued till the adjournment for tea.

On Saturday, Professor Loewenstein (Glasgow) demonstrated his theories on the anterior drainage system of the human eye by a series of beautiful slides. Mr. J. Minton (London) discussed occupational diseases of the eye in the glass and metal industries, caused by the short infra-red rays, incidentally showing the enormous decrease in glassblowers cataract since the introduction of automatic machinery in the bottle industry, and the high incidence of cataract among chain makers which is still a manual industry. Dr. Gunnar von Bahr described a method of accurate measurement of the thickness of the living cornea and its variations in response to solutions of varying osmotic pressure. His experiments supported the theory of Cogan and Kinsey bearing on the circulation of fluid in the cornea and its purpose in its metabolism. Dr. Winifred Fish (Oxford) read a paper on "hereditary mesodermal dystrophy," and Miss Margaret Dobson (London) on "dynamic retinoscopy."

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## FACULTY OF OPHTHALMOLOGISTS

The following have been elected as Officers of the Faculty for 1948-49:—

*President*: Sir Stewart Duke-Elder; *Vice-President*: Mr. J. J. Healy; *Honorary Secretary*: Mr. Frank W. Law; *Honorary Treasurer*: Mr. O. M. Duthie.

The following Standing Committees and Sub-Committees have been elected:—

*Constitution*: Mr. F. A. Juler (Chairman and Convener), Mr. George W. Black, Mr. J. J. Healy, Mr. W. H. McMullen, Professor W. J. B. Riddell; *International Relations*: Mr. F. A. Juler (Chairman and Convener), Mr. R. C. Davenport, Mr. J. H. Doggart, Miss Ida Mann, Professor W. J. B. Riddell; *Medico-Political*: Mr. J. D. M. Cardell, Mr. J. H. Doggart, Sir Stewart Duke-Elder, Mr. P. Jameson Evans, Mr. R. Affleck Greeves, Mr. J. J. Healy, Mr. E. F. King, Mr. Frank W. Law, Mr. E. G. Mackie, Dr. John Marshall, Mr. A. S. Philips, Mr. J. N. Tennent, Mr. David Wilson; *Education and Research*: Mr. R. C. Davenport (Chairman and Convener), Mr. J. Foster, Mr. E. F. King, Mr. T. Keith Lyle, Miss Ida Mann, Professor W. J. B. Riddell, Dr. George Scott.

The Officers are *ex-officio* members of all Committees.

*Representatives of the Faculty on the Prevention of Blindness Committee, National Institute for the Blind*: Mr. J. H. Doggart, Sir Stewart Duke-Elder, Mr. Humphrey Neame, Mr. D. Stenhouse Stewart, Mr. Maurice Whiting; *Representatives of the Faculty on the Ophthalmic Group Committee, British Medical Association*: Mr. J. D. M. Cardell, Mr. J. H. Doggart, Mr. R. Affleck Greeves, Mr. E. F. King, Dr. R. S. MacLatchy, Mr. J. N. Tennent.

Mr. J. H. Doggart has been co-opted to the Council of the Royal College of Surgeons of England for 1948-49 as the representative of the Faculty.

Representatives of the Faculty have met representatives of the Ministry of Health to discuss several points connected with the Supplementary Ophthalmic Service, including the use of drugs by opticians. The Ophthalmic Benefit Approved Committee have recently authorised the use of certain drugs by opticians in National insurance work. The Faculty's representatives have made it clear that they are strongly opposed to the use of drugs by opticians, and the Ministry officials, while not committing themselves, have suggested that for the Supplementary Eye Service no regulations about the use of drugs by opticians should be laid down, but that a Commission, which has been appointed to consider registration of opticians, should make a decision on the matter. The standard of vision required on examination by opticians and the need for a report to the patient's general medical practitioner if that standard

was not attained has also been considered. The Faculty's representatives put forward the opinion that 6/6 for each eye examined should be the standard. The Ministry officials considered that this would be too high a standard for incorporation into regulations, and agreed that guidance on this matter should be given in a handbook to be issued to opticians, the relevant portion being first submitted for the Faculty's comments.

The question of whether ophthalmologists should see patients in their own consulting rooms under the Supplementary Ophthalmic Service has been discussed by the Council. It is the policy of the Faculty that state patients should be seen in Clinics under the Supplementary Service or in Hospital Clinics under the Permanent Service, and that this latter Service should be inaugurated as soon as possible, because it is the Faculty's view that no Supplementary Ophthalmic Service Clinic should take place in Hospital. Where there is no Clinic available, it will presumably be unavoidable for patients to be seen in private consulting rooms under the Supplementary Ophthalmic Service though it is likely that this practice will result in a destruction of private practice.

Nominations for Ophthalmic Services Committees of Local Executive Councils throughout the country have been discussed with Mr. Grey Turner of the British Medical Association. Various fusions, modifications and additions have been agreed, which will all appear on the final list.

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## BOOK NOTICES

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**Modern Trends in Ophthalmology.** Edited by A. SORSBY. 600 pages. 169 figs. London, Butterworth & Co., 1948. Price 63/-.

The second volume of "Modern Trends" follows on the lines of its predecessor and is equally good. Forty-eight articles are included, arranged in sections—physiology, diagnostic procedures, pathology, treatment and social aspect of ophthalmology. They touch practically every aspect of the specialty which has shown progress during recent years and at the same time fill a number of gaps left in the previous volume. The editor has drawn widely from many countries for his contributors among whom are to be found many from most countries of Europe and America. Not only has the choice been wide but it has also been good. Able and impartial editing is seen in the readability of all the sections, the exclusion of well-established information and the inclusion of only new points of view. The volume will be found most useful to those wishing a short resumé of recent progress.

Introduction to Physiological Optics. (Einführung in die physiologische Optik). By A. v. TSCHERMAK-SEYSENEGG. 2nd Edition. 213 pp. Springer, Vienna. 1947.

On certain aspects of the physiology of the eye v. Tschermak may be ranked as the greatest living authority, in particular on such abstruse problems as torsion and its perspective distortion of an after-image following movements of the eye, and perhaps more so on space perception; it is therefore of value to have, within the span of two hundred odd pages, a concise summary of present day knowledge of these aspects of physiological optics. The book also contains disquisitions on other branches of the subject: visual acuity, adaptation, after-images and colour vision including colour-blindness. In these last-mentioned sections the author seems not to have been able to draw to any great extent on the wealth of material in the British and American literature of the past ten to fifteen years (Hecht, for example, is barely mentioned; Hartline not at all); the book is thus very little more than a restatement of the author's earlier contributions to Bethe's Handbook. Valuable as these contributions were at the time, their main use now is as a source of references to the classical work and it may be that the author has been unwise in attempting to abridge them so as to bring them within the compass of this small book. If, instead, he had expanded his treatises on the eye movements and space perception and had provided also a thoroughgoing analysis of image-formation by the eye and its aberrations, the book would have been transformed into one of real value for the modern reader; as it is, the abbreviated accounts of these subjects are very difficult indeed to understand. The book contains references only to the author's earlier reviews on physiological optics to which the reader is referred for individual references to the literature.

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## OBITUARY

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HENRY SMITH, C.I.E., Lieut.-Col., I.M.S., ret.

THE death of Lieut.-Col. Henry Smith in Ireland was announced in March, 1948. He was 91 years of age and few of his contemporaries can now be left alive. Smith received his medical education in Ireland and qualified M.D., M.Ch., in 1888.

In the early years of the present century the name of "Jullundur" Smith was on all ophthalmological lips. His enormous experience in cases of cataract in India led him to devise the intracapsular operation of extraction and in this he did pioneer work.

The advantages to the Indian peasant were obvious:— only one stay in hospital, one operation, no return for needling; and with so many illiterate patients, a glass for general use could be ordered almost as soon as the eye was white. In successful cases the surgeon was relieved of the bugbear of tags of capsule left to be incarcerated in the healing wound. Loss of vitreous was the item around which most of the criticism of this new operation centred.

Smith made a large section in the corneo-scleral junction; he cut no conjunctival flap; he performed a large iridectomy and delivered the lens by pressure on the lower part of the cornea with the blunt tip of a strabismus hook. The suspensory ligament was ruptured in the first place and the lens either "tumbled" or pushed straight out. In Smith's hands the results were good. He always insisted on the importance of having a properly trained assistant and spent much time and trouble in training his own.

Outside India the ophthalmological fraternity was critical of the operation. Surgeons in England, in particular, were concerned at the large loss of vitreous that sometimes occurred. When the writer first went to Moorfields as a clinical assistant he got the impression that the intracapsular operation was considered unjustifiable in view of the grave risks involved.

Smith was quite unperturbed by this criticism and went on with his work. He introduced a hook for the lens delivery in certain cases, published many papers in the *Lancet*, *Ind. Med. Gaz.*, and *Brit. Med. J.*, and summed up his experiences in a monograph on the treatment of cataract.

As time went by modifications were made in the operation, notably that of Barraquer, of Barcelona, who employed a suction pump for the lens delivery and nowadays the operation of intracapsular extraction is performed all over the world. The credit of this must go in the first place to Henry Smith for his pioneer work.

After leaving Jullundur, Smith worked as Civil Surgeon at Amritsar until he retired from the service and came to live at first at Sidcup, and later in Ireland.

The writer remembers Smith visiting Moorfields about forty years ago. He was a large man, with a massive head and not very approachable to juniors. Of our contemporaries who visited India to work with Smith we recall Basil Lang, who was greatly impressed by his stay at Amritsar.

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## NOTES

**Appointments:** MR. JAMES H. DOGGART has been co-opted a member of the Council of the Royal College of Surgeons of England for the ensuing year to represent Ophthalmology.

Mr. R. J. Buxton, M.B., has been appointed ophthalmic surgeon to the Yeovil District Hospital.

\* \* \* \*

**American Ophthalmological Society: Officers** THE American Ophthalmological Society elected new officers at its recent meeting at Hot Springs, Virginia, for the current year: *President*—Dr. Bernard Samuels, New York; *Vice-President*—Dr. Parker Heath, Boston; *Secretary-Treasurer*—Dr. Maynard Wheeler, New York.

\* \* \* \*

**Blindness in British African and Middle-East Territories** A REPORT of a joint committee appointed by the Colonial office and the National Institute for the Blind, following the visit of a Delegation to Africa and some Middle-East Territories between July, 1946, and March, 1947, has been published and can be obtained from H.M. Stationery Office.

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**Back Numbers of the Journal** THE British Journal of Ophthalmology requires copies of the Journal for January, 1942, August and October, 1946, in good condition. Anyone having spare copies to dispose of should inform the manager.

\* \* \* \*

**The Illuminating Engineering Society.** THE following officers for the next session are announced:—*President*—Mr. J. M. Waldram; *Vice-Presidents*—Dr. E. C. Walton, Mr. E. W. Murray, Dr. J. N. Aldington; *Hon. Treasurer*—Mr. J. G. Holmes; *Hon. Secretary*—Mr. H. C. Weston; *Hon. Editor*—Mr. W. R. Stevens.

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## THE GOLDMAN ANGLE-REDUCTION PRISM AND GONIOSCOPY CONTACT-GLASS FOR USE WITH A SLIT-LAMP

For slit-lamp examinations of the posterior parts of the eye some means of reducing the angle between the inspection and illuminating beams is required. This want is met by the four-sided prism illustrated herewith (Fig. 1) devised by

Fig. 1

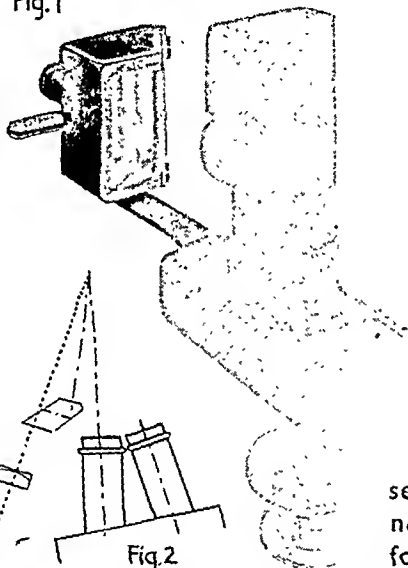


Fig. 2



Fig. 3

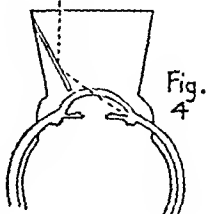


Fig. 4

Prof. Hans Goldman of Berne University, which can be supplied suitably adapted for use on any type of slit-lamp. As will be seen in the diagrammatic illustration (Fig. 2) the prism displaces the angle by  $5^\circ$ , which is usually as much as is necessary. The light beam remains in exactly the same adjustment as when examining the anterior sections of the eye, and there is no loss in the facilities for sharp focussing with the microscope.

For examination of the angle of the anterior chamber Professor Goldman has devised a CONTACT GLASS for use with the angle reduction prism (Fig. 3). The diagrammatic illustration (Fig. 4) shews how it makes possible the examination of the entire iridial angle without any alteration in the adjustment of either the slit-lamp or microscope, by rotating it around the corneal axis.

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SIR JOHN HERBERT PARSONS  
C.B.E., D.Sc., LL.D., F.R.C.S., F.R.S.

# THE BRITISH JOURNAL OF OPHTHALMOLOGY

SEPTEMBER, 1948

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## COMMUNICATIONS

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SIR JOHN HERBERT PARSONS

An Appreciation

BY

PROFESSOR E. D. ADRIAN, O.M., F.R.S.

**I**N this tribute to Sir John Parsons for his 80th birthday the contributors are all, with one exception, ophthalmologists or his former pupils. The exception is the writer of this introduction, who has never had the privilege of his teaching and knows next to nothing of clinical ophthalmology. Yet a physiologist may claim the right to join with pathologists and clinicians in any volume covering the whole field of Sir John's activities. His scientific studies of the problems of vision have meant so much to us and to psychologists, too, that we must not be denied the pleasure of wishing him well.

It has never been easy to combine the busy life of a consulting physician or surgeon with research into the basic problems of natural science, though fortunately exceptional people have managed to do it in the past and are doing it even now. But it must be still more difficult to remain both the recognised authority on the science and the recognised leader in the practice of a branch of medicine, to remain our foremost authority on the physiology of vision as well as the dominant figure in the British School of Ophthalmology, and in this School not only the teacher but the organiser of teaching and research, the adviser of governments, and the expert whose opinion is indispensable in all the varied problems where human vision is concerned. This is the position which Sir John Parsons has held for many years. Physiologists may grudge some of the time he has had to spend in the wards and committee rooms, and clinicians may have wished for even more of his help, but neither can deny his outstanding position in the science and practice of ophthalmology.

His early training certainly qualified him for the work he has done. The influence of Lloyd Morgan at Bristol and of Schafer at University College might have kept him to the narrower path of academic psychology or physiology. Though his wide interests and general kindness must be innate, the years spent in general practice were surely not wasted: we can still go to him with our troubles and feel the better for his advice. And when he finally turned to ophthalmic surgery what better surroundings could he have found than those at Moorfields and at University College Hospital?

I have no right to speak of the influence which he has had in these two centres of scientific medicine, but I can speak of the influence of his writings on all physiologists who have studied the sense organs. His book on colour vision was first published in 1915 and has remained our surest guide through the intricacies of a fascinating subject. The great originator of it all, Sir Isaac Newton, did not like hypotheses and Thomas Young's three colour

theory ran very close to the facts which he discovered, but from the time of Goethe to the present day the subject has been beset with speculation and the proportion of new theories to new facts has been dangerously high. Sir John's book was a masterly analysis of the facts and an unbiassed examination of the theories, both rare delights. Much of the material was assembled for the first time and given orderly presentation and meaning. His book soon became the classical work of reference on colour vision and its redressing of the balance between fact and theory gave a new impetus to the subject. The impetus has remained and much of the present day interest in colour vision can be traced to this source.

Having reviewed the physiology of vision Sir John showed his wide knowledge of the border lands of neurology and psychology in his "Introduction to the Theory of Perception." In this, too, he brought together a wealth of information and showed its relevance to the general problem. But though these two books are the concrete expression of his work in the field of academic science they are by no means his sole contribution to it. He has achieved as much or more by his personal influence, by his constant and powerful advocacy of research on visual physiology, and by his kindly support of the young research worker. His colleagues in the Royal Society and on the Medical Research Council know him as a wise and honest councillor with the initiative needed for the planning of new developments and the experience needed for carrying them through. His pupils and friends everywhere know him as one who inspires their warm affection as well as their admiration for what he has done. We offer him our most cordial greetings and our sincere congratulations on his birthday.

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## SIR JOHN HERBERT PARSONS

*An appreciation*

BY

Professor J. VAN DER HOEVE

SIR JOHN HERBERT PARSONS reaches the age of 80 years on September 3rd of this year. His whole life has been devoted to his and our beloved profession; ophthalmology in England is greatly the gainer for his work and his reputation is truly international.

His writings on all aspects of ophthalmology are numerous and well known; and in addition to his professional activities, he served his country, both in war and in public life in peace, in many capacities. For these services many honours were accorded to him. My tribute to him, however, is essentially concerned with the work he has done for the International Council of Ophthalmology, a sphere wherein we worked together and where I knew him best. After the first World War an Anglo-American Convention of Ophthalmology was held in 1925 when a Committee for reviving the International Congresses was nominated. The English members of the Committee were Treacher Collins, Sir John Parsons and Leslie Paton. As a result a meeting was held at Scheveningen in 1927, where there gathered 50 oculists from 25 different nations, and here the plans were laid for the Congress of 1929. It is interesting that we met again afterwards in the same year (1927) when we each received the degree of Ll.D. at Edinburgh.

In the name of the oculists who serve on the International Council of Ophthalmology, I wish from the very bottom of my heart that Sir John will still have many more years of good health and happiness.

## SIR JOHN HERBERT PARSONS

## An Appreciation

BY

R. R. JAMES

*"Time hath, my Lord, a wallet at his back,  
Wherein he puts alms for oblivion ;"*

TROILUS AND CRESSIDA, ACT 3, SCENE 3.

ULYSSES, in the play, calls the wallet a "great-siz'd monster of ingratitude."

In my case the wallet holds no ingratitude ; but as one gets older it naturally becomes fuller and fuller. It will, however, never be so full that I can forget all I owe to Sir John Parsons. It is now more than forty-one years since I was first introduced to him at one of the evening meetings of the Ophthalmological Society by a common friend. I have never forgotten how he said, when he was informed that I was hoping to come and work with him at Moorfields, that ophthalmology was already overfull. He must have noticed the chagrin in my looks for he quickly added : "Of course there's always room for a good man."

I became his clinical assistant at the end of the year 1907 and have been intimately associated with him for more than thirty years. I bear to none of the companions on life's journey so much real, almost filial, affection as I do to Sir John Parsons. He has been a most strong Tower to British Ophthalmology and especially to the Journal, standing ever,

"Four-square to all the winds that blew."

That he may long continue to be the Doyen of our branch of the profession is the fervent desire of all who have been associated with him.

## DEVELOPMENTAL APHASIA

Also known as Congenital Word-blindness and  
sometimes referred to as Alexia or Dyslexia

BY

A. H. H. SINCLAIR

EDINBURGH

THIS remarkable developmental failure is met with in various sensory-motor affections and may be manifested in functional failure in connection with sight, hearing, kinaesthetic performance and probably in other functional activities.

We are here concerned with developmental aphasia connected with vision, also referred to as congenital word-blindness. This disability is met with in children but does not become obvious until the child has been confronted with the problem of learning to read. The condition does not depend on the degree of general intelligence but is met with in all grades of natural ability, including occasionally individuals of the highest intelligence, which renders it all the more important that the nature of the disability should be clearly recognised. It does not depend on failure of vision due to errors in refraction or difficulty in focusing, or other causes found in the eye, though such should always receive treatment when present. This condition is a failure in visual comprehension, caused by delayed development of unilateral hemispherical dominance and failure in word-memory and relates to the psychology of vision: letters and words are seen but not recognised. Fortunately aural perception is available and eagerly used by children suffering from this visual embarrassment and proves to be of great value to them.

There is a natural tendency to recovery in all children so affected which increases progressively with the child's development and education. The condition may be mild and transitory or severe and difficult to overcome. The cases form a graded series, including all degrees of severity. In the milder cases recovery often takes place in the ordinary course of school education: in the more severe cases persistent skilled instruction, undertaken early, is essential. In the Edinburgh Primary Schools about 10 per cent. of the children were found to be affected by developmental aphasia, of whom half recovered in the ordinary course of school education, while the remainder required special treatment.

Teachers of children may fail to recognise the fundamental cause of the symptoms and this was appreciated by Hinshelwood in 1896 when he wrote: "It is a matter of the highest importance

to recognise the true nature of this difficulty in learning to read . . . otherwise these children may be harshly treated or punished for a defect for which they are in no wise responsible." The thwarting effect of this disability, especially in highly intelligent children in whom it often appears, gives rise to emotional disturbances which vary according to the temperament of the child and may produce inferiority complex, a defiant attitude to instruction, carelessness or inattention from hopelessness and sometimes fits of crying. The connection between such symptoms and their fundamental cause has frequently remained unrecognised by teachers; but is evident to the trained observer.

Developmental aphasia has doubtless always been present amongst schoolchildren, though unrecognised, and an outstanding example of this would seem to be provided by the early life-history of the famous surgeon, John Hunter. Up to the age of 17, Hunter showed very clearly that he was in every respect, apart from book-learning at school, a highly intelligent boy, possessed of character and a great desire to understand the facts and the mysteries of the natural objects of country life in the midst of which he grew up. It was only when he was confronted with learning to read, that is, to comprehend facts and ideas through the recognition of printed symbols, that he failed to progress. He was sent to a good school where his older brothers, James and William, had excelled, but John could not learn to read. All his biographers insist on this remarkable fact in John Hunter's early life. In addition it is recorded of him that he suffered from prolonged fits of crying after he was beyond the age when such evidence of emotional distress is met with in boys.

The failure to learn to read and write in the case of a boy of John Hunter's ardent and enthusiastic temperament and the knowledge that his brothers had succeeded so well at the same school must have caused him great disappointment and distress.

He was the youngest in a family of ten and lived in a cultivated and intellectual circle where all enjoyed the advantages of learning from books, but John Hunter was denied this source of knowledge for which he possessed such an insatiable appetite. Nobody could understand why he failed to learn to read and write, when he could and did learn so much through other channels, by actual contact with phenomena, by the observation of things and by hearing others talk or read. His own recorded words are: "When I was a boy I wanted to know about the clouds and the grasses, and why the leaves changed colour in the autumn: I watched the ants, bees, birds, tadpoles and caddis worms; I pestered people with questions about what nobody knew or cared anything about." The enthusiasm of his genius, however, impelled him into the new fields of

personal observation and study in which he later so greatly excelled.

Only in the light of knowledge which was not possessed until 150 years later could the true nature of John Hunter's disability have been recognised as an example of developmental aphasia.

But even in modern times these cases may remain unrecognised: for example, in the case of Ronald Hall, of which he himself has given a valuable and interesting account in the *Brit. Jl. Ophthal.*, September, 1945. He says, "I can speak from experience when I say what a terrible handicap this is for a child. Although in World War No. 1 I spent over three years at the Front, I can truthfully say that I never during those years experienced a fraction of the stark terror that I did as a boy at school during English lessons lest I should be called upon to read aloud and reveal to the whole class that I could not do so." He was taken to an oculist but the condition was evidently not recognised, as glasses were prescribed but produced no effect. He tells how he recovered spontaneously at the age of 15 and emphasizes that it was not want of intelligence on his part, as he passed first into the Civil Service as a young man.

The first account of this disability appeared in the *British Medical Journal*, when in 1896 Morgan<sup>x.1</sup> published the case of a boy of 14 who could not learn to read, though he had no difficulty with figures: the schoolmaster said of him that if the instruction had been aural this boy would have been the smartest in the school. Words written or printed seemed to convey no impression to his mind. Morgan writes to Hinshelwood, "It was your paper—may I call it your classical paper—on acquired word-blindness and visual memory published in 'The Lancet'<sup>x.2</sup> which first drew my attention to the subject, and my reason for publishing this case was that there was no reference anywhere, so far as I knew, to the possibility of the condition being congenital."

Hinshelwood's paper, to which Morgan refers, describes in detail several cases of acquired word-blindness in adults suffering from disease of the brain, of which the following is an interesting example, illustrating the parallel between this condition and congenital word-blindness, i.e., developmental aphasia:—

"The patient, an inspector of schools, a highly intelligent and educated man, was familiar with four languages, English, French, Latin and Greek: he had become word-blind and could no longer read English. When, however, I put a Greek book into his hand, he was both surprised and delighted to find that he could read it correctly: it was evident then that so far as Greek was concerned there was no sign of word-blindness. With Latin there were evidences of partial word-blindnesses and with

French even more so. The word-blindness in English was not absolutely complete—there was no letter blindness and short words here and there could be picked out. Thus the word-blindness extended to only three of the four languages: Greek had entirely escaped. He also read numbers with fluency and correctness. He read musical notes as fluently and as correctly as ever."

We know that there are separate symbolisations for different languages, music, drawing and the like.

Two weeks after Morgan's paper in 1896, Hinshelwood published his first communication on Congenital Word-blindness in the form of a critical note, explaining some of the symptoms in the case reported by Dr. Morgan, in the light of his knowledge of the phenomena of acquired word-blindness, and four years later, in 1900, he gave the first analysis and explanation in detail of the symptoms met with in this condition in order "to establish the diagnosis on a scientific basis and to show that the difficulties encountered in teaching children so affected to read could be overcome by patient and persistent training."

Hinshelwood published his book on Congenital Word-blindness in January, 1917.

In 1901 Nettleship<sup>x.3</sup> having expressed his indebtedness to Hinshelwood for his exposition of the subject, gave notes of five cases of great difficulty or inability to learn to read which had come under his observation and been recognised by him clinically years earlier, though not published, notes of two of which are given. The first of these cases was a boy aged 11, who was brought to him in March, 1882, because he was extremely slow in learning to read and it was supposed that his eyes might be at fault. Immense pains had been taken in trying to teach him to read and he was very anxious to learn. Nettleship was surprised to find that his difficulty was quite as great with words of No. 10 Jaeger and even No. 16 as with No. 1. It was not want of accommodation, for neither the size of the print nor the distance at which the book was held had any influence on the result. He knew some words pretty well, but unless he recognised a word at sight, he took a very long time to spell it: if, however, he was helped by having the word spelt out to him quickly he pronounced it at once. . . .

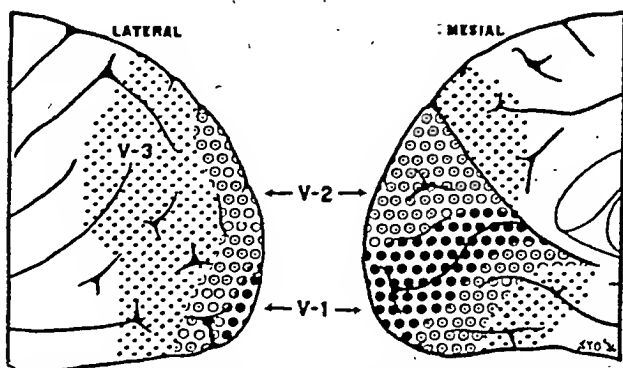
The second case, also a boy, was brought in 1882: he had great difficulty in learning to read print, though he could read music well and showed considerable facility in drawing. What puzzled his parents was that he hardly knew even short words when he spelt them: he understood what was read to him but not what he read himself. It was found in this case also that large type was not read any better than small: his manner of reading was more

suggestive of incomprehension than bad sight. After an enormous amount of patience and perseverance the boy learnt to read easily.

Nettleship finally says, "Whatever may be the anatomical cause of this condition, its importance from an educational point of view both positively and negatively is obvious. If the defect is curable, the remedy will doubtless be found in methodical and persevering instruction in reading, begun at the earliest possible age.

Although it is not intended to attempt a review of the literature on this subject, some reference must be made to the more recent work. In 1936 Professor Rönne of Copenhagen<sup>x.4</sup> gave an address on Congenital Word-blindness in School Children, in which he confirms Hinshelwood's experience of this disability occurring in families and refers to the case of a woman who had suffered from developmental aphasia as a child and became the mother of six children, all of whom also suffered from the same disability. He had also met with the condition in three generations of the same family. He describes his method of isolating affected children from their normal school fellows. He deplores the fact that "this quite characteristic condition is almost unmentioned in either common medical literature or in the ophthalmological."

Samuel Orton,<sup>x.5</sup> Iowa, U.S.A., who in 1925 had written a very interesting paper dealing mainly with Left-handedness and Mirror-reading and writing in children, published in 1937 his book, "Reading, Writing and Speech Problems in Children." This work is based upon an extensive experience in American schools and is the most detailed and authoritative account of Developmental Aphasia which has appeared.



An outline map of the lateral and mesial surfaces of the occipital region of the left hemisphere of a human brain showing the distribution of the three chief types of visual cortex. From *Reading, Writing and Speech Problems in Children*. S. T. Orton (W. N. Norton & Co., N.Y., 1937).

In describing the occipital visual centre, Orton distinguishes (1) visual perception, (2) visual recognition, (3) visual association and defines the broad outlines of the respective cerebral fields with illustrations.

His interpretation of word-blindness is an excellent extension of Head's concept of speech as "Symbolic thinking and expression." The word "Strepho-symbolia" is used by Orton to indicate a deficit in psycho-visual orientation which he was able to identify in a number of cases.<sup>x.5a</sup>

Emphasizing the importance of treatment in cases of developmental aphasia, Orton says: "The reading disability cases as a group form a clear-cut example of the appearance of emotional disturbances which are purely secondary to the academic obstacle. When, however, proper treatment is not instituted or the handicap is entirely disregarded because of the 'Laissez-faire' attitude adopted by many schools, the feeling of inferiority is very apt to extend to other fields so that the child approaches every task in the expectation of failure and all of his school work may lag seriously behind." He advises, however, that "failure in learning to read with understanding must not be considered a specific disability unless it is out of harmony with the child's skill in other fields—notably the ability to learn by hearing."

The research which was initiated under the Ross Foundation in Edinburgh in 1938<sup>x.6</sup> was not undertaken because the subject was new, but because it had not received attention in the Edinburgh Primary Schools (the laissez-faire attitude mentioned by Orton!). While it was found in the course of these investigations that nearly 10 per cent. of children in the Primary Schools showed evidence of this disability, only about half that number required special tuition, the others recovering under the usual school training.

Miss M. Macmeeken, M.A., B.Ed., Ph.D.,<sup>x.7</sup> who carried out the research for the Ross Foundation, has as a psychologist been very successful in the education of children suffering from developmental aphasia: she considers the undertaking one for a specialist only: the willing co-operation of the child must be secured and subjects selected with a view to maintaining the lively interest of the pupil who takes part in the work with the teacher alternately in writing and reading. Not only is good method necessary but an extended period of time is required to secure the result. Three school terms are usually found necessary.

In considering the underlying causes of this disability it would seem to fall into two parts which, while they react upon each other, are distinct:—

(a) Mirror reading and writing, twisting of syllables and confusion of certain letters and palindromic words, relating to



insufficiently developed dominance in one of the cerebral hemispheres: these earlier manifestations (as above noted) frequently disappear in the first few years of school life.

(b) Failure in word memory, which tends to be a more permanent and stubborn difficulty to be overcome: this may relate to the delayed development of myelination of cortical neurons, with associated delayed function.

A reference to this subject of myelination occurs in a paper which appeared in the Transactions of the Royal Society of Edinburgh in 1913<sup>x.8</sup> by the late Alexander Bruce, M.D., LL.D., F.R.C.P.E., and James W. Dawson, M.D., from which I quote: "If it is true that every cell differentiates in view of a function, it is necessary to remember that it is the functioning which determines and perfects the cell differentiation. The nerve paths in the embryo remain as embryonic nerves till the function of the tract is called into play: influences which accelerate or retard the period at which nerve fibres are brought into functional activity have also an effect in determining the date of complete axial fibril and myelin differentiation. Margulies<sup>x.9</sup> has pointed out that in the newly-born kitten, if the eyelids on one side are carefully opened, the optic nerve on that side myelinates before that of the opposite side excluded from the light, and numerous other instances might be given where the completion of differentiation is related to the completion of function. The fibres in the distal end of a non-united nerve remain for a very considerable time as embryonic nerve fibres, but when secondary suture is carried out they very rapidly effect a complete differentiation—in a period of time in which it would have been impossible for axis-cylinders to grow out from the central to the distal end. The differentiation proceeds, therefore, *pari-passu* with the functioning which is its determining cause. Ballance and Stewart<sup>x.10</sup> think that some stimulus, afforded by the conducting impulses, is necessary in order to admit of the full development of the nerve fibres."

I wish here to express my indebtedness to A. Ninian Bruce, M.D., F.R.C.P.Ed., Lecturer on Physiological Neurology, University, Edinburgh, for directing my attention to the above-noted research in which he took part with his father.

In an address entitled "Some Recent Advances in the Study of the Brain as the Implement of Mind,"<sup>x.11</sup> Professor R. J. A. Berry, M.D., F.R.C.S., discussed myelination in the normal and the abnormal brain. This prompted me to write to Professor Berry and to look up his former work on this subject. From his book, "Brain and Mind," 1928, the following passage seemed to have a special bearing on the possible significance of myelination in developmental aphasia: "Flechsig has shown that myelination

does not occur simultaneously in all parts of the nervous system, but is later in proportion as the nerve fibre (axon of the neuron) is more recent in the phylogenetic history of the animal. Not only are the entering receptor neurons of the spinal cord more numerous than the outgoing effector neurons, but they develop or myelinate earlier, in order that they may function earlier. Generally speaking, the same holds good for the neo-pallial cerebral cortex, and the last of the cortical neurons to myelinate are those associating or linking together the association areas of the cortex, and these are precisely the areas which are universally regarded as being the seats of the higher mental processes. But if these same areas are not stimulated by suitable incoming receptor impulses, their association neurons will not myelinate and consequently the areas remain throughout life veritable "silent" areas, to the detriment of the mentality of the individual.

It consequently follows, and it is a strikingly significant fact, that the general order of acquisition of the nerve properties essential to life are:—

1. Transmission of entero-ceptive impulses from viscera by means of both non-medullated and medullated fibres through the autonomic nervous system.
2. Transmission of proprio-ceptive impulses, concerned in locomotion.
3. Transmission of extero-ceptive impulses such as touch, pressure, sight hearing, etc.
4. The last series of neurons to myelinate, that is to function, are those of the cortex which correlate and control the incoming extero-ceptive impulses, and extend them through the association areas, thus making possible education, speech thought and reason. If the neurons of this series fail to myelinate, there must follow an impairment of intelligent action and a reaction to the environment on a lower plane.

The period of time occupied by the myelination of these four great developmental series is a long one, but differs very considerably in different individuals. It commences before birth and goes on, in the educated classes, until well on into middle life, because education, that is, the constant submission of the cortical association areas to appropriate incoming receptor impulses, is a powerful stimulus to the internuncial association cortical neurons. In the non-educated classes the process of myelination of these neurons ceases much earlier in life, and as a consequence they do not attain the same degree of intellectuality.

The importance of myelination is also borne out by pathology for it is a significant fact that in *multiple* or *insular sclerosis* of the

brain and cord, the axis cylinders of the areas affected remain intact whilst the myelin sheaths are destroyed. The disturbances of co-ordination accompanying this condition may, therefore, be an expression of a loss of insulated conduction.

In considering myelination in relation to the differentiated cortical visual fields, Orton refers to Flechsig's work as follows:

"Flechsig found that maturation proceeds in three distinct waves covering, in separate stages, those areas of the brain cortex whose destruction leads to the three syndromes of cortical blindness, mind blindness and word blindness and the comparable conditions in audition. Flechsig demonstrated that at the time of birth only the "arrival platforms" or first level cortices have received their myelin, that a second period of myelinization follows during the first two or three months after birth which results in the ripening of the second zone of cortex lying near by each arrival platform and that only during the final or third wave does maturation occur in the areas of the third level."

He continues: "I have emphasized this dissection of the cerebral functions into steps because it offers us some understanding of how a selective loss of reading, for example, in the adult, or a selective retardation in learning to read in a child, may occur with full visual competence in other regards."

Developmental aphasia is an isolated disability. The diagnosis is difficult and uncertain in mentally defective children, but clearly recognisable in children otherwise normally developed in relation to age. The characteristic mental defects are related to difficulties in symbolisation and in word-memory: all other faculties of recognition and recollection are normal.

All expert and experienced teachers of such children are agreed that encouragement, patience, perseverance and time are necessary and in advancement the pupil must make the pace. In all this the most important element in securing progress lies in oft-repeated practice (in reading and writing) by performance on the part of the pupil. This activity on the part of the child fulfils the requirements of cerebral stimulation referred to by Bruce and Berry in relation to the development of function.

I suggest that the localized delay or failure in the development of myelination of internuncial nerve fibres in the cerebral cortex is the most probable explanation of this developmental failure in learning to read.

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## HISTOLOGICAL FINDINGS IN A CASE OF ANGIOID STREAKS

BY

F. H. VERHOEFF

BOSTON, MASS.

FOR the privilege of making this report I am indebted to the late Dr. Grady E. Clay. It deals with the microscopic examination of one eye removed after death from a patient with angioid streaks in both eyes. The eye was removed under the direction of Dr. Clay and sent by him to Dr. Algernon Reese for sectioning. A complete set of celloidin sections was prepared and stained under Dr. Reese's supervision and then sent to me at the request of Dr. Clay. The hospital at which the patient died was the Grady Memorial Hospital of Atlanta, Georgia, and to the authorities of this institution I am indebted for complete copies of the hospital records including the autopsy report on this patient. The clinical record was signed by Guh H. Adams, M.D. The autopsy was performed by Abner Golden, M.D., and the report signed by Walter H. Sheldon, M.D., pathologist. For the purposes of this paper the following summary of these hospital records will suffice:

The patient, a 50-year-old coloured female was admitted to the Grady Memorial Hospital, Atlanta, Ga., Jan. 28, 1944. She was known to have had syphilis which was inadequately treated. However, the Kahn test was negative at the final admission to the hospital although in 1935 the Wassermann test was 4 plus. She was known to have had hypertension since 1935. In 1939 the blood pressure was recorded as 200/110 and at this time she began to experience intermittent oedema of the ankles. There were not marked symptoms, however, until three

weeks before present admission when she became short of breath, orthopneic, and had several attacks of paroxysmal nocturnal dyspnea and a cough productive of thin white sputum. Peripheral edema became marked. The temperature was 100°, pulse 110, respiration 30, blood pressure 140/100. The patient was in respiratory distress and the neck veins were distended. There was dullness to percussion over the right lung base where many medium and fine rales were heard. The heart was markedly enlarged to the left, and there was a systolic murmur at the apex. There was a diastolic gallop. The liver was enlarged to palpation, and tender. Reflexes were normal.

Dr. Clay observed and later reported to me a fact not noted in the hospital record, namely, that the patient had pseudo-xanthoma elasticum, a condition with which he was thoroughly familiar. On ophthalmoscopic examination Dr. Clay found a few angioid streaks in both fundi. He intended to give a detailed description of the streaks, but the patient died before he could do so. He recorded in addition that "the media were clear, the nerve heads normal. The retinal arterioles showed Grade 2, arteriosclerosis, and Grade 1 angiospasm."

The patient received digitalis and other cardiac therapy, but failed to respond. She died on her seventh hospital day.

At autopsy, extensive old and recent infarcts of the lungs were found. The branches of the pulmonary artery showed old and recent thrombosis, and some showed complete recanalization. The heart showed extensive old and recent infarction, and mural thrombi, displaying varying degrees of organization were present in both ventricles. The heart weighed 580 gms. and was dilated. The aorta throughout its length displayed a rather marked degree of arteriosclerosis and numerous calcified atheromatous plaques. The viscera showed chronic passive congestion and there was extensive central haemorrhage and necrosis of the liver, and recent infarction of the spleen. Of interest also, was thrombosis of the right transverse sinus of the dura mater.

Incidental findings included leiomyomata of the uterus and a small paraovarian cyst. Microscopic examination of the heart, lungs, spleen, pancreas, liver, kidneys, showed generalised arteriosclerosis. The sclerosis included branches of the coronary arteries.

Cultures obtained at autopsy showed no growth from the lungs and coagulase negative staphylococcus aureus from the blood.

The left eye, removed 11 hours after death, was fixed in 10 per cent. formalin. The celloidin sections made horizontally through the entire eye included the whole of the optic disc and a considerable extent of the fundus above and below it. The sections were thin, well stained in alum haematoxylin and eosin, and unusually free from artefacts. After careful examination, selected sections were dismantled to me and restained by my elastic tissue stain<sup>1</sup> and by other methods.

The globe shows no distortion in the sections, and the choroid and retina are everywhere *in situ* except for a slight artificial separation of the retina anterior to the equator on the temporal side. The optic nerve and disc are normal. At the margin of the disc there are two large conglomerate colloid excrescences, each about 0.10 mm. in diameter, one on the nasal side in the mid-plane, the other on the temporal side below. The former contains two minute blood vessels (Fig. 1). Otherwise the retina is normal. There is marked peripheral cystoid degeneration, but this is no greater than that often seen at this age. The rods and cones show the usual distortion seen in normal eyes removed post mortem. The choroid is so slightly shrunken by the fixation that the details

of its structure are easily seen. It is normal except for the changes in Bruch's membrane next described, and a few insignificant foci of lymphocytes. The elastic tissue of its stroma is neither increased nor diminished in amount, and stains normally. The



FIG. 1.

Vascularized colloid excrescence at margin of disc. The basophilic Bruch's membrane is also well shown. H. and E. Photo.  $\times 180$ .

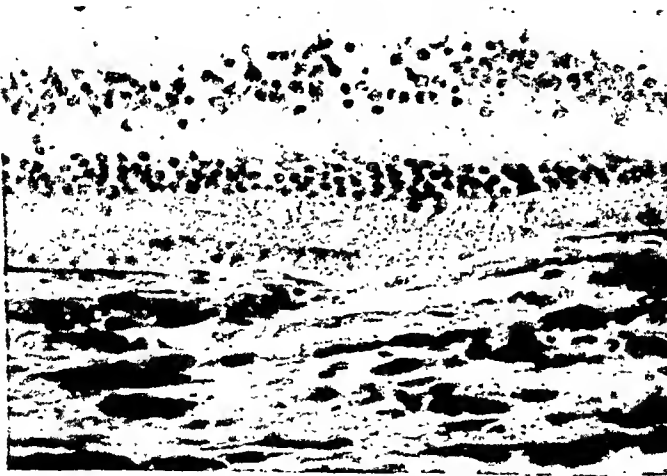


FIG. 2.

Wide gap in basophilic Bruch's membrane—oblique section of angioid streak. The pigment epithelium shows some post mortem disturbance and the chorio-capillaris is not well shown, but both are intact. A few new cells have been formed at the margins of the gap. Elastic tissue stain. Photo.  $\times 360$ .

whole uvea and the sclera are more heavily pigmented than in the eye of a white person, but less so than in the eye of a pure-blooded negro.

Bruch's membrane in the posterior fundus stains strongly in haematoxylin, that is to say, is basophilic. The basophilia is continuous about half way to the equator on each side, then becomes patchy as in Fig. 2 of Verhoeff's and Sisson's paper,<sup>2</sup> and finally ceases near the equator. However, even where it is continuous the basophilia is not uniform, but makes Bruch's membrane appear to vary considerably in thickness at frequent intervals. This indicates that originally the basophilia was patchy here as it is now towards the periphery. On the nasal side of the eye a wide gap is seen in the basophilic membrane in every section that includes the upper half of the optic disc. Reconstructed from the sections, the gap begins at the upper margin of the optic disc, courses nasally downward and reaches the horizontal mid-plane at a distance of 4 mm. from the disc margin. Here the gap is 0.24 mm. wide in the section. Below this level the gap is no longer seen, probably because it has become horizontal. In one place in the middle of the gap a short stretch of basophilic membrane remains, as if the membrane had ruptured in two places close together. At its narrowest place the gap is 0.06 mm. wide in a section. In all sections the pigment epithelium and the choriocapillaris are intact at the site of the gap, and appear to be normal except that the epithelium shows slight post-mortem changes. In some sections these two structures are bulged slightly forward, in others slightly backward (Fig. 2) through the gap. This displacement is no doubt artificial. In a few sections there are within the gap several new formed spindle-cells just beneath the pigment epithelium (Fig. 2). Some of these are pigmented. The edges of the gap are not square, but always more or less pointed, suggesting that the gap resulted from a rupture at a relatively weak place in the basophilic membrane.

In addition to the wide gap just described, two other gaps are found in Bruch's membrane. Each of these is very minute, only 0.009 mm. wide, and is seen in only 4 consecutive sections. One is on the temporal side 0.45 mm. from the disc, the other on the nasal side 1.0 mm. from the disc (Fig. 3).

In the anterior part of the eye a pathological finding of possible importance is a localized exuberance of elastic tissue at the corneal limbus on each side in the horizontal meridian (Fig. 4). This elastic tissue is even more abundant than that generally found in a beginning pterygium, shows less degeneration than is usually found in pingueculae, and is not to any extent basophilic.

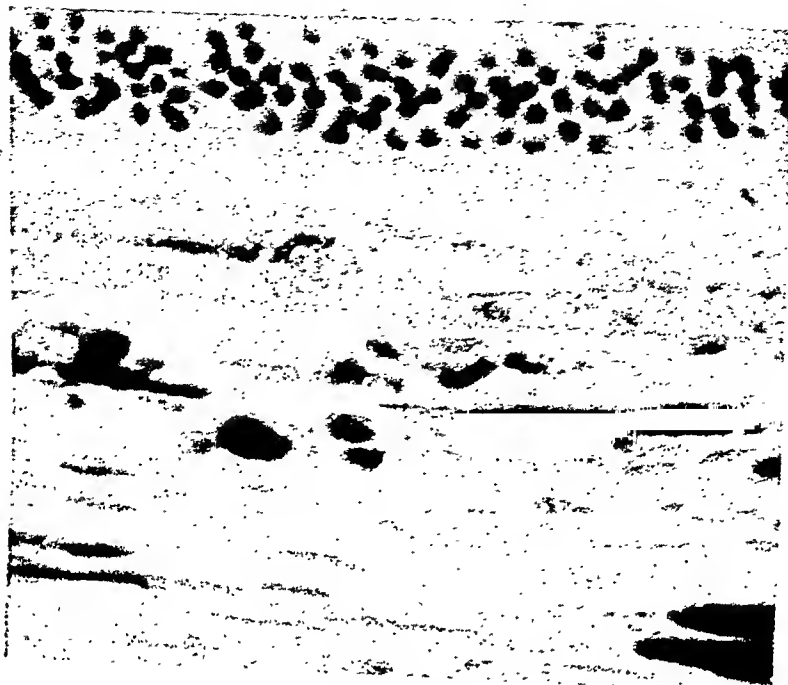


FIG. 3.

Minute gap in basophilic Bruch's membrane. H. and E. Photo.  $\times 675$ .



FIG. 4.

Exuberant elastic tissue (pinguecula) at corneal limbus, nasal side. Elastic tissue stain. Photo.  $\times 70$ .





FIG. 5.

Concretion in epithelium of pars plana of ciliary body. A similar concretion was found in another section. H. and E. Photo.  $\times 152$ .

The cornea, iris, and lens are normal. The ciliary processes show hyaline change, consistent with the age of 50 years. Two sections some distance apart, each shows a fairly large concretion within the epithelium of the pars plana (Fig. 5). The sclera, including its elastic tissue, is normal and free from calcific deposits. The intra-ocular vessels, including those of the choroid and retina, show no definite sclerosis. Some of the choroidal arteries, owing to their post mortem collapse, appear to have unusually thick walls. The posterior ciliary vessels seen in the vicinity of the optic nerve are also free from sclerosis.

#### COMMENT

The only abnormal histological findings in the fundus of this eye, aside from the two drusen at the margin of the optic disc, were the basophilia of Bruch's membrane and the gaps in this membrane. Other than the wide gaps, seen on the nasal side in the sections, there was nothing to account for the angioid streak that had been seen ophthalmoscopically. It is especially noteworthy that the pigment epithelium and chorio-capillaris were intact at the site of the gap. Allowing for the fact that the streak was sectioned obliquely, its real width was probably about 0.10 mm. to 0.05 mm. The two other gaps found were too minute to have been seen ophthalmoscopically, but probably in the course of time would have widened and lengthened. In other words, they probably indicated how angioid streaks begin.

To explain, on the basis of these findings, the ophthalmoscopic appearance of an angioid streak, one must assume that Bruch's

membrane, especially when basophilic, obscures the chorio-capillaris and contributes to the brightness of the fundus by reflecting a considerable amount of light. Within a gap, this reflection is absent, and the light is largely absorbed by the chorio-capillaris. Thus the appearance of a streak is due to increased visibility of the choroid, especially the dark red chorio-capillaris, exposed beneath the pigment epithelium at the site of a gap. This explains why in certain cases Dr. Clay has been able to obliterate the visibility of a streak by pressure upon the eye, for such pressure might express the blood from the chorio-capillaris. It is interesting that in the present case one of the sections in the middle of a gap showed an island such as occasionally is seen ophthalmoscopically in cases of angioid streaks. No doubt it resulted from Bruch's membrane rupturing at two places close together.

Böck<sup>3</sup>, in 1938, reported the microscopic findings in two eyes, removed 48 hours post mortem, which ophthalmoscopically had shown numerous typical angioid streaks. Hagedoorn<sup>4</sup>, in 1939, reported similar microscopic findings in two eyes also removed post mortem. In Hagedoorn's case the ophthalmoscopic examination was unsatisfactory, so that his microscopic findings would have been of doubtful significance were it not for the fact that they agreed with Böck's. Recently, Klien<sup>5</sup> has reported the microscopic findings in two eyes in which angioid streaks had been found ophthalmoscopically. Her findings were essentially the same as those described by Hagedoorn. These observers noted that Bruch's membrane stained deeply in alum haematoxylin and found breaks in the membrane. Apparently none of them was aware of the findings of Verhoeff and Sisson<sup>2</sup>, noted below, although Hagedoorn used the term "basophilia" and found a senile eye in which this condition of Bruch's membrane existed. Böck thought that the gaps in the membrane would be ophthalmoscopically invisible if the pigment epithelium remained intact over them. Hagedoorn's explanation of the ophthalmoscopic appearance of the streaks was similar to that given above by me.

In 1928 I reported finding microscopically<sup>6</sup>, on the inner surface of the choroid of an enucleated eye, numerous small ridges. As seen microscopically these appeared as dark streaks similar in size and distribution to angioid streaks. In addition, I found changes in the macula that seemed to accord with those often seen ophthalmoscopically in cases of this condition. I felt sure, therefore, that the ridges were angioid streaks. Since such ridges were absent in Böck's, Hagedoorn's, Klien's, and the present case, I am compelled to abandon this view and to believe that my case was a highly unusual one in which the ophthalmoscopic picture would have closely simulated that of angioid streaks. It

can now be regarded as certain that angioid streaks are gaps in an altered Bruch's membrane. Kofler<sup>7</sup> astutely surmised this fact 27 years ago without histological evidence, but it was never generally accepted.

Many years ago I observed that in certain eyes Bruch's membrane stained deeply in alum haematoxylin, and in 1926 with Dr. Sisson made a special investigation of this phenomenon<sup>2</sup>. We found it in 60 out of 600 eyes selected at random, termed the condition of the membrane basophilia, and assumed it was due to calcification. Since we found it in no eye under 48 years of age, we concluded that it was a senile condition. We also concluded that it was not necessarily related to any other pathological condition in the eye.\*

Bruch's membrane is generally described as consisting of two layers, an inner cuticular and an outer elastic layer. But behind the elastic layer, and also no doubt filling its interstices, is a thin layer of connective tissue which, as I have pointed out<sup>2</sup>, could be regarded as a third layer. Perhaps a more accurate way to describe Bruch's membrane is to say that it consists of an inner epiblastic cuticular layer produced by the pigment epithelium, and an outer mesoblastic layer composed of collagen abundantly pervaded in its inner portion by fine elastic fibrils. These fibrils are coarser near the optic disc and here extend entirely through the mesoblastic layer and continue into the underlying choroidal stroma. In thick cross sections, and often even in thin sections after formalin fixation, it is difficult or impossible to distinguish the two layers, the membrane appearing as a rather thick single layer. When the membrane is basophilic, this condition, if slight, often can be seen to involve only the elastic tissue, but if marked, it seems to involve the whole thickness of the membrane. Nevertheless even when the basophilia is marked, plane sections may show individual elastic fibrils. In its early stages the basophilia is not continuous, but is seen in cross sections in the form of long spindle-shaped spots resembling elongated nuclei. These appearances are depicted in the paper<sup>2</sup> referred to.

In many eyes I have found Bruch's membrane throughout its thickness abnormally eosinophilic and hyaline, and not at all

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\* Mrs. Helenor Wilder has recently sent me from the Army Institute of Pathology in Washington sections of five eyes with such basophilia, from patients aged respectively 39, 32, 26, 25 and 20 years. In four of the eyes the basophilia was very slight and there were no breaks in the membrane. However, angioid streaks might have developed later. The other eye (aged 25 years) shrunken and degenerated as the result of an old injury, showed marked basophilia of Bruch's membrane and breaks indicative of angioid streaks. The possibility of angioid streaks existing in the fellow eye of this patient was not excluded. It is unlikely that the degeneration of this eye was an essential factor in the calcification of Bruch's membrane, since in many other similarly degenerated eyes I have not found such calcification.

basophilic. In some eyes it is both basophilic and eosinophilic, but I have not yet determined whether it is always eosinophilic when it is basophilic. However, I suspect this to be true and that in sections stained in both haematoxylin and eosin the basophilia hides the eosinophilia. I also suspect that basophilia is always preceded by eosinophilia of Bruch's membrane. In the present case, in sections that are stained only lightly in haematoxylin it is easily recognizable that Bruch's membrane is both eosinophilic and basophilic. Unna called degenerated elastic tissue which stained in haematoxylin, elacin. It has been found this gives the differential staining reactions of calcium, and often in addition those of iron. It is evident, therefore, that basophilia of Bruch's membrane means calcification of this membrane as I originally assumed. The basophilia of elacin elsewhere, however, is seldom if ever as intense as it often is in Bruch's membrane. Böck found that in his case the membrane stained differentially for calcium but not for iron. Hagedoorn found that it stained differentially for iron but not for calcium and attributed failure of the calcium test to acidity of the formalin used in the fixation. Klien found that the membrane gave the Kossa reaction for calcium and the Turnbull blue reaction for iron.

That basophilia of Bruch's membrane sometimes occurs in senile eyes is not surprising, for degeneration and calcification are characteristic of old age. But according to Holloway<sup>8</sup> almost half of the cases of angioid streaks have been observed before the age of 40, and 4 cases before the age of 20. Since vision is not appreciably impaired by the condition until the onset of macular changes, no doubt many of the cases were not discovered until long after streaks had formed. Hence in cases of angioid streaks, basophilia of Bruch's membrane is not dependent upon age. Nor is it necessarily dependent upon defective calcium metabolism, for degenerated tissues readily undergo calcification even in young normal individuals. Hagedoorn assumed that the basophilia was due to "precocious senility of the elastic fibres" of the body.

Two closely related questions now arise. First, what causes gaps in basophilic membrane? Second, why are angioid streaks not associated with the basophilia that often occurs in senile eyes? The second question was not discussed by Böck, Hagedoorn, or Klien, evidently because they were unaware of the fact that basophilia of Bruch's membrane is a common senile condition. Theoretically a gap could be caused by complete dissolution of Bruch's membrane at a localized site. But microscopically there is no evidence for this. It seems certain that the membrane has ruptured and that the broken edges have separated, leaving the

other tissues apparently unaltered. Assuming, as also seems certain, that the basophilia is due to calcification, it is obvious that a basophilic membrane could be fractured by voluntary movements of the eye, winking, and "rubbing the eye" by the hands. Widening of the gaps probably results not from elasticity of the membrane, because calcification would do away with its elasticity, but from the elasticity of the choroid as a whole. Presumably this elastic tension not only widens and extends the gaps but contributed to their original cause. In senile eyes, it is reasonable to suppose that the choroid has largely lost its elasticity long before the membrane is calcified. Hence angioid streaks do not usually result when fractures of Bruch's membrane occur in senile eyes—the broken edges do not tend to separate and may even tend to override each other (Fig. 1, Verhoeff and Sisson<sup>2</sup>). That angioid streaks occur chiefly in the vicinity of the optic disc is no doubt explained by the fact that basophilia is always most marked here. This may be because, as I have already pointed out, Bruch's membrane is normally somewhat different in this vicinity than elsewhere. Why, in cases of angioid streaks, and in many senile eyes, this membrane alone of all structures of the choroid should undergo calcification is not obvious. Possibly this fact is partly dependent upon the close relation of the membrane to the chorio-capillaris.

A feature characteristically associated with angioid streaks is a mottled appearance of the fundus. Probably this is due to unevenness and discontinuities such as seen microscopically in the basophilia of Bruch's membrane in the present case. The marked proliferative changes within and along the gaps in three of the cases explain the white borders and ophthalmoscopic appearances of some of the older streaks. Such proliferative changes may also explain the disappearance of streaks. In none of these cases was there any reformation of Bruch's membrane.

Haemorrhages described as choroidal or sub-retinal are frequently seen in cases of angioid streaks. Since the haemorrhages often occur early in life, it seems to me probable that they are usually not due to local vascular disease, but to fracture of the calcified Bruch's membrane causing rupture of the chorio-capillaris. In some cases the rupture and haemorrhage might not result immediately from the fracture, but later from widening of a streak. If the pigment epithelium was not ruptured, the blood could lift it up in the form of a mound and later become organized into solid tissue. When occurring beneath the macula this process would result in the condition known as disciform degeneration of the macula. As first demonstrated by Verhoeff and Grossman<sup>9</sup> and soon afterwards but less conclusively by Braun<sup>10</sup>,

senile disciform degeneration of the macula is typically produced by haemorrhage beneath the pigment epithelium.

In addition to the streaks, mottling of the fundus, and sub-retinal haemorrhages, other fundus changes often occur in cases of angioid streaks. It is believed that macular changes will ultimately occur in every case if the patient lives long enough. Only exceptionally do these macular changes take the form of the typical disciform degeneration just mentioned. In the present case the fundi, including the maculae, were normal except for the streaks. This was true also of Böck's case, with the exception that there was some slight formation of new tissue on Bruch's membrane elsewhere than in the macula. Only Hagedoorn's and Klien's cases afford histological information as to the late fundus changes. The findings in their cases were remarkably alike. In each, both maculae were involved, and in similar fashion—there was a thick layer of vascularized tissue on the inner surface of Bruch's membrane. This tissue was very old and in each case showed foci of ossification in one eye. In both cases similar tissue was also present elsewhere in the fundi. Klien described in addition, the widespread formation of a thick cuticular layer by the pigment epithelium. On the basis of her histological findings she satisfactorily accounts for the fundus pictures in five clinical cases of angioid streaks.

Aside from the streaks themselves, and possibly the deeply seated haemorrhages, none of the fundus changes seen in cases of angioid streaks is peculiar to this condition. Thus the vascularized tissue, found by Hagedoorn and Klien between Bruch's membrane and the pigment epithelium, may occur in eyes without angioid streaks, and without basophilia of Bruch's membrane. Most commonly it occurs in senile eyes, but is not necessarily associated with local vascular changes. Brown<sup>11</sup> has called special attention to it. Vessels enter this tissue through holes in the membrane. These holes are not due to fractures of the membrane, for usually it is not basophilic. I assume that they result from penetration of the membrane by capillary sprouts which develop into arteries and veins. Sometimes this tissue is formed beneath the macula and produces a condition that ophthalmoscopically would be difficult to distinguish from the typical senile disciform degeneration due to haemorrhage. In fact, in Hagedoorn's and Klien's cases I am unable to decide this question even by the microscopical evidence.

Since in cases of angioid streaks, cardio-vascular disease often develops, it is probable that in some of the cases disciform degeneration of the macula is dependent upon vascular disease just as it usually is in ordinary senile cases. Haemorrhages

within the retina, and circinate retinitis, occurring in association with angioid streaks, are no doubt due to vascular disease. Klien attributes almost if not all the changes in the fundi in cases of angioid streaks to calcification of Bruch's membrane. Thus she says "The clinical picture of angioid streaks represents not only the visible ruptures in Bruch's membrane but also the multiform end results of irritation of pigment epithelium and chorio-capillaris by the sharp, calcified edges and fragments of the broken membrane." With this view I cannot fully agree. For as already indicated I have seen in eyes showing no basophilia of Bruch's membrane the changes she attributes to irritation by calcified membrane. Among these changes she does not mention sub-retinal haemorrhage, which, as I have suggested above, may result from fracture of the calcified membrane.

In the present case at the margin of the disc there were two large "colloid excrescences" ("Drusen"), one of them vascularized. Böck and Hagedoorn also noted "Drusen" on the discs in their cases. Such formations are typically senile, that is to say degenerative in origin, but it is impossible to maintain that degeneration of elastic tissue has anything to do with them. Klien found "several hyaline bodies in the temporal half of the left nervehead." It would seem, therefore, that in cases of angioid streaks there is not only degeneration of Bruch's membrane, but sooner or later also degeneration of the pigment epithelium and various proliferative changes associated therewith. A degenerative process noted in the present case but not in the other three cases, was the formation of concretions in the pars ciliaris retinae (Fig. 5).

On each side of the eye examined in the present case there was a large pinguecula. Hagedoorn noted a large pinguecula on one eye in his case. Böck and Klien noted no pingueculae in their cases, but may not have looked for them. As a matter of fact, a section kindly sent me by Dr. Klien shows a pinguecula on the nasal side of the left eye—she did not section the anterior part of the right eye. Histologically, a pinguecula except in size is essentially identical with a lesion of pseudo-xanthoma elasticum. But since both conditions are similar to senile elastoses of the skin the only relationship between them may be that both are degenerative conditions.

It is noteworthy that in all four of the cases in which the eyes have been examined microscopically, death was due to cardiovascular disease. In Böck's case the patient was a male, aged 44, in Hagedoorn's a female, aged 48, in Klien's a male, aged 53, and in the present case a female, aged 50. Pseudo-xanthoma

elasticum was absent only in Klien's case. In the present case, although there were evidences of marked general arteriosclerosis of the larger vessels, the vessels of the retina and choroid, and the posterior ciliary vessels seen in the sections, showed no definite sclerosis. Böck also found, with the exception of one choroidal artery, the retinal and choroidal vessels free from sclerosis, but found marked sclerosis of the posterior ciliary arteries. He thought that the atheromatous changes in the aorta in his case were primarily due to degeneration of elastic tissue. Hagedoorn in his case found slight thickening of the walls of the choroidal arteries but no intimal proliferation. No autopsy was done in his case. Klien's findings were substantially the same as Hagedoorn's. It would seem that in none of the four cases were vascular changes in the choroid or retina sufficiently marked to account for any other lesions in the eyes.

There are three conditions that have been associated with angioid streaks too often to be merely coincidental, namely, cardio-vascular disease, pseudo-xanthoma elasticum, and Paget's disease. Holloway<sup>8</sup> found that cardio-vascular disease was noted in 23.3 per cent. of the cases he collected from the literature. Actually it may have been overlooked in many of the other cases. This fact suggests that vascular disease will finally develop, and at a relatively early age, in every case of angioid streaks. Clay<sup>12</sup> found pseudo-xanthoma elasticum in 30 per cent. of his cases of angioid streaks. Apparently I was the first to note angioid streaks in a case of Paget's disease<sup>6</sup>. Twelve such cases have been reported to date but these may give an inadequate idea of the frequency of the association, for Terry<sup>13</sup> found three cases of angioid streaks in 22 cases of Paget's disease. Paget's disease is typically associated with general arteriosclerosis, but no case has been reported in which it was associated with both angioid streaks and pseudo-xanthoma elasticum.

It requires great stretching of the imagination to assume a common systemic cause for angioid streaks, cardio-vascular disease, pseudo-xanthoma elasticum, and Paget's disease. It is true that some of the elastic tissue in pseudo-xanthoma becomes basophilic, but there is first marked hyperplasia of the elastic tissue and this does not occur in the case of Bruch's membrane. As regards Paget's disease, Klien suggests that in this disease the angioid streaks may have a different origin, in that calcium is deposited in a normal Bruch's membrane. I can explain the associations in question only by assuming that the four conditions are independently abiotrophic and when they occur together do so as the result of hereditary linkages.



## CONCLUSIONS.

Angioid streaks result from ruptures of a basophilic Bruch's membrane. The gaps are widened by the elastic tension of the choroid. In the ophthalmoscopic picture the basophilic condition (calcification) brightens the contiguous fundus and makes conspicuous the dark red chorio-capillaris exposed beneath the pigment epithelium by the ruptures. The streaks are later often altered in appearance by proliferative changes along or within them. The similar ruptures that occasionally occur in senile eyes do not widen into visible streaks, probably because the senile choroid loses its elasticity before Bruch's membrane becomes calcified.

Other lesions that occur in the macula and elsewhere in the fundus in cases of angioid streaks are usually due to proliferative changes involving the pigment epithelium, such as occur under senile degenerative conditions. The subretinal haemorrhages in the macula and elsewhere may be due to fractures of the calcified membrane causing ruptures of the chorio-capillaris. When such a haemorrhage lifts up the pigment epithelium in the macula, "disciform degeneration" results. Haemorrhages arising within the retina, are probably explained as is also circinate retinitis, by the vascular changes that commonly occur in cases of angioid streaks.

The association of angioid streaks in many cases with pseudo-xanthoma elasticum, in some cases with Paget's disease instead, and in still other cases with neither of these conditions is difficult to explain, as is also their association with cardio-vascular disease. A possible explanation is that these associations are dependent upon hereditary linkages.

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A CONTRIBUTION TO THE MICROSCOPICAL  
ANATOMY OF THE SYMPATHIZING EYE

BY

R. AFFLECK GREEVES

IN comparison with the number of existing publications concerned with the microscopical anatomy of the exciting eye in sympathetic ophthalmitis, those dealing with the sympathizing eye are relatively few. In most ophthalmological text-books indeed, it is stated that the character of the histological changes found in exciting and sympathetic eyes is identical.

The subject of this communication is a number of sympathizing eyes which I have had the opportunity of examining after they had been sectioned. These are 13 in number, they have been collected from different sources, and their history, I think, leaves no doubt as to the true nature of their pathological condition; in all of them the original perforating injury to the exciting eye was an intraocular operation.

The order in which I have arranged this series of cases corresponds to the particular length of time which elapsed between the date on which inflammatory signs were first observed in the sympathizing eye and that on which it was enucleated in each case. In Case 1 this period was the shortest, and in case 10 it was most prolonged. In the 3 cases which I have placed last on the list, the exact duration of this period, although undoubtedly a long one, is somewhat uncertain.

A study of the foregoing cases shows that the particular character of the inflammatory changes occurring in sympathizing eyes is not related to the duration of the disease, and that this statement also applies to the distribution of such changes in the various ocular tissues. Nor can any relationship be found between either of these factors and the length of time elapsing between the injury to the exciting eye and the onset of inflammation in the sympathizing eye.

In 7 cases the infiltrating inflammatory cells were purely lymphocytes and plasma cells, in 6 cases epithelioid cells were present and in 3 of the latter, giant cells appeared. The only constant factor common to all these cases is the presence of an irido-cyclitis which varied considerably in character and intensity. The choroid was found to be normal in 5 cases, while in 6 cases areas of infiltration were found consisting of lymphocytes and plasma cells only. Epithelioid cells occurred in the choroid in 2 cases, and giant cells in one case only. These areas of choroidal

infiltration consisted of localized patches, always situated in the outer layers of the choroid, the capillary layer being free except in one case, No. 13, in which the whole thickness of the choroid was involved. Also the posterior section of the choroid, that immediately surrounding the optic disc, was consistently the most densely infiltrated part. Both these findings are in accordance with the conditions usually found in exciting eyes and I regard them as salient characteristics of sympathetic disease.

The vitreous showed some inflammatory cells in most cases.

The optic nerve was normal in 5 cases and oedematous in 8 cases in which the sheaths of the central vessels showed lymphocytic infiltration.

The optic nerve sheath was infiltrated in one case only and the sheaths of the ciliary vessels in 4 cases.

An interesting point is the spontaneous rupture of the lens capsule which was found in 3 cases, in none of which had there been any operative interference. In 2 of these cases, in both of which the disorganized iris and swelling lens matter were jumbled together in a necrotic mass, the intra-ocular pressure was low, while in the third the tension was raised.

Organized plastic exudate in the anterior chamber was found in 3 cases in which no operative interference had been undertaken and its occurrence does not support Fuchs' view that plastic exudation in exciting eyes affected with sympathetic disease is due to secondary infection and not part of the specific process.

In none of the cases did such infiltration as was present in the iris show any particular tendency to be situated in the posterior layers, and no Fuchs-Dalen bodies were seen.

From a study of these 13 cases I think it is reasonable to draw the conclusion that no special characteristic of the sympathetic inflammatory process is invariably found in the sympathizing eye on microscopical examination.

*Case 1.* Male, age 60 years. Signs of sympathetic uveitis were observed 5 weeks after operation on the other eye. Enucleation was performed 3 months later because the eye became glaucomatous and painful.

*Microscopical appearances.*—Scattered nodular lymphocytic and plasma cell infiltration of the iris, with a few epithelioid cells in some of the nodules. Slight lymphocytic infiltration of the ciliary body. The anterior uveitis was not plastic in character. Nodular lymphocytic and plasma cell infiltrations were present in the outer layers of the choroid in the neighbourhood of the optic disc. No epithelioid or giant cells were seen. Retinal vessels, optic disc, vitreous and ciliary vessels and nerves were free from infiltration.

*Case 2.* Female, age unknown. Signs of sympathetic uveitis appeared 2 months after operation on the other eye and an iridectomy was performed for the relief of secondary glaucoma. The eye was enucleated 3½ months after the first appearance of inflammatory signs.

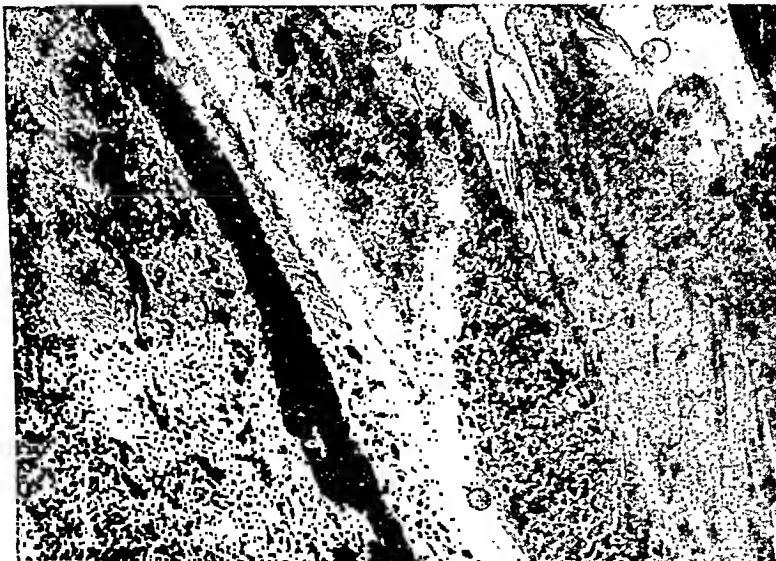
*Microscopical appearances.*—A layer of lymphocytes was present on the posterior corneal surface, and nodular lymphocytic infiltration of the iris and ciliary body;



*Photo by E. V. Willmott*

FIG. 1.

Showing nodular lymphocytic infiltration in the posterior layers of the choroid in Case 1. The retinal detachment is an artefact.



*Photo by E. V. Willmott*

FIG. 2.

Showing the ruptured lens capsule in Case 3, and the invasion of the lens substance by inflammatory cells.

no epithelioid cells were seen. There is slight lymphocytic infiltration of the choroid near the optic disc. The central vessels and larger retinal vessels show marked lymphocytic infiltration in their sheaths. The ciliary vessels also show some lymphocytic infiltration. There is scattered lymphocytic infiltration in the vitreous.

*Case 3.* Female, age 49 years. Signs of sympathetic uveitis were observed 3 months after operation on the other eye, and 5 months later the eye was enucleated because of secondary glaucoma.

*Microscopical appearances.*—Dense coagulum was present in the anterior chamber and dense infiltration, mainly lymphocytic, in the iris, with a few epithelioid and giant cells in the denser nodules. There is much plastic exudation, with an organized membrane in the pupil. The ciliary body shows dense lymphocytic infiltration with a few epithelioid cells. Localized patches of plasma cells, lymphocytes, and a few epithelioid cells occur in the outer layers of the choroid near the optic disc. There is some lymphocytic infiltration round the central vessels. The ciliary vessels and nerves also show some perivascular infiltration. The optic nerve and its sheath are also invaded by lymphocytes. The lens capsule is ruptured, with invasion of the lens substance by inflammatory cells.

*Case 4.* Male, age 60 years. Signs of sympathetic uveitis were observed 2 months after operation on the other eye. Enucleation took place 5 months later because of secondary glaucoma, for which a paracentesis had already been performed.

*Microscopical appearances.* Plastic exudate, partly organized, is present in the anterior chamber. Lymphocytic and plasma cell infiltration only is seen in the iris and ciliary body. The choroid and optic nerve are normal. The vitreous is slightly infiltrated anteriorly.

*Case 5.* Female, age 54 years. Signs of sympathetic uveitis were observed 3 months after operation on the other eye. 10 months later the eye was enucleated because of secondary glaucoma for which a paracentesis had already been done. Dense lymphocytic and plasma cell infiltration occur in the iris and ciliary body, and a similar type of nodular infiltration is seen in the outer layers of the posterior choroid. The optic disc shows infiltration with lymphocytes anteriorly and there is lymphocytic infiltration of the sheaths of the larger vessels. No epithelioid or giant cells are observed. No ciliary vessel or nerve infiltration is seen. The vitreous shows a few scattered inflammatory cells.

*Case 6.* Female, age 59 years. Sympathetic uveitis was observed 1 year and 5 months after operation on the other eye, and 11 months later, when the eye was shrinking it was enucleated. The iris and ciliary body are mainly disorganized, and represented by a mass of granulation tissue containing lymphocytes, plasma cells, epithelioid and giant cells. The choroid shows localized areas of lymphocytic infiltration posteriorly, but no epithelioid or giant cells. The optic disc shows lymphocytic infiltration in the sheaths of the central vessels. The sheaths of the ciliary vessels and nerves are also infiltrated. The vitreous is detached and infiltrated. The lens capsule is ruptured.

*Case 7.* Male, age 70 years. Sympathetic uveitis was first observed a year after operation on the other eye. Enucleation took place a year later because of secondary glaucoma.

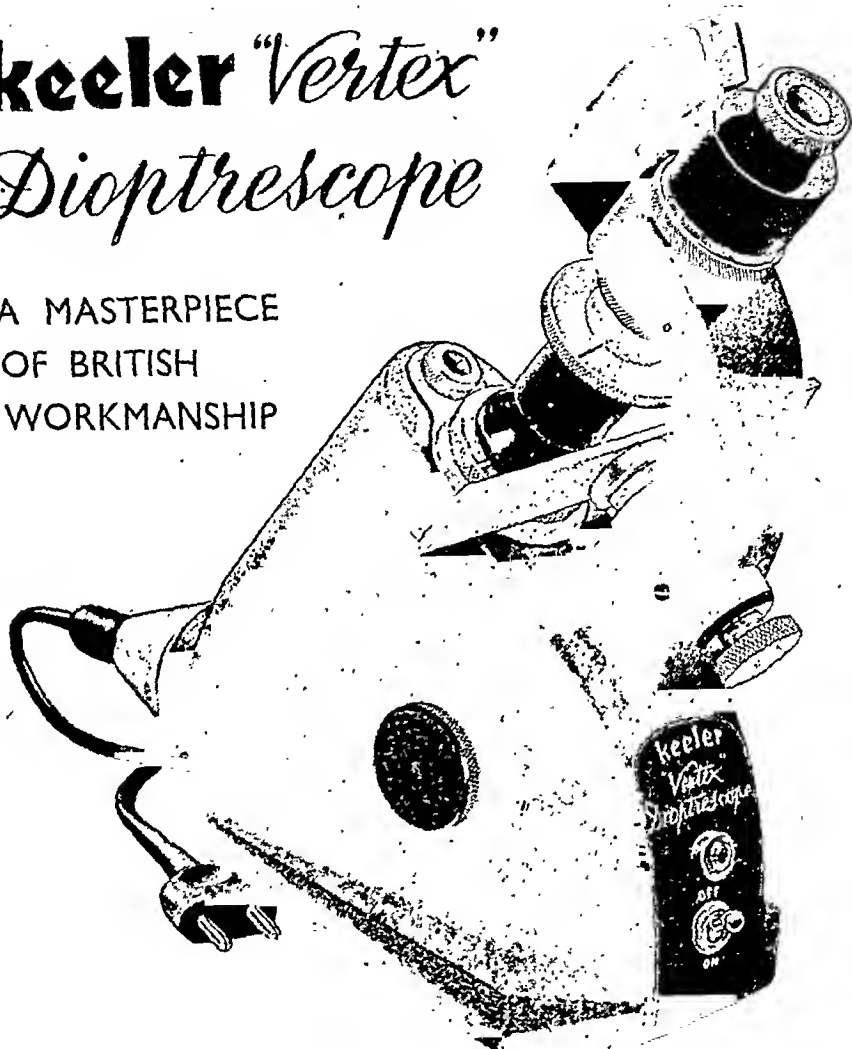
*Microscopical appearances.*—Plastic exudation almost fills the anterior chamber, but some K.P. can be seen. The iris and ciliary body show scattered infiltration, with lymphocytes and plasma cells. In the posterior part of the choroid are localized patches of lymphocytes and plasma cells, but no epithelioid cells. The optic disc, central vessels, and ciliary vessels and nerves are normal. A few inflammatory cells are seen in the vitreous.

*Case 8.* Female, age 64 years. Signs of sympathetic uveitis were observed 5 months after operation on the other eye. 1 year and 3 months later, the eye was enucleated because of secondary glaucoma, for which a paracentesis had already been performed.

*Microscopical appearances.*—Organized exudate is seen in the anterior chamber. The iris and ciliary body show nodular infiltrates with lymphocytes and plasma cells, but no epithelioid cells. The choroid is normal. The optic nerve is cupped

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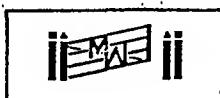
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and atrophic with a few lymphocytes in the sheaths of the larger vessels. The ciliary vessels, nerves and vitreous are normal.

*Case 9.* Male, age 70 years. Signs of sympathetic uveitis were observed 4 months after operation on the other eye. Enucleation took place 16 months later.

*Microscopical appearances.*—Nodular infiltration of the ciliary body and iris, with lymphocytes and plasma cells, and epithelioid cells, but no giant cells are seen. The choroid, ciliary vessels and nerves are normal. There is some infiltration of the larger vessels on the optic disc and some inflammatory cells in the anterior vitreous.

*Case 10.* Age, sex, and other particulars unknown. Enucleation took place 18 months after operation on the other eye. The eye was then shrinking.

*Microscopical appearances.*—Coagulum was present in the anterior chamber. The iris and ciliary body were mainly disorganized and showed dense lymphocytic and plasma infiltration with some epithelioid cells. No giant cells were seen. The choroid and optic nerve were normal as well as the ciliary vessels. The lens capsule was ruptured.

*Case 11.* Female, age 50 years. The dates are uncertain, but the eye was excised over 4 years after the operation on the other because it was then blind and painful. The iris and ciliary body show nodular lymphocytic and plasma cell infiltration, with no epithelioid cells. The choroid is normal. The optic nerve and the sheaths of the larger vessels are infiltrated anteriorly. The ciliary vessels and nerves are free from infiltration. The vitreous shows many inflammatory cells.

*Case 12.* Female, age 67 years. The eye was enucleated 9 years after operation on the other eye, because it became blind and painful.

*Microscopical appearances.*—The iris and ciliary body are slightly infiltrated with lymphocytes and plasma cells, polymorphonuclears are visible in the anterior chamber. Some nodular lymphocytic infiltration occurs in the posterior part of the choroid in its outer layers. The vitreous is clear. The optic nerve was not seen.

*Case 13.* Female, age 55 years. A left iridectomy was performed. The right



Photo by E. V. Willmott

FIG. 3.

Section showing the choroid in Case 13. Dense infiltration with lymphocytes and epithelioid cells. The retinal detachment is an artefact.



eye became painful and glaucomatous some weeks later and was trephined 4 months after the original operation on the left eye. It was enucleated a month later.

*Microscopical Sections.*—This eye is the only one of the series which shows all the characteristics recognized as peculiar to advanced sympathetic disease in an exciting eye. The whole of the uveal tract is a mass of granulation tissue in which all types of inflammatory cell are seen, and which shows nodules containing epithelioid and giant cells. The central vessels, optic disc, and the nerve sheath, as well as the ciliary vessels and nerves, are infiltrated with lymphocytes. The lens capsule is ruptured, but in this case the rupture may have occurred when the operation for the relief of secondary glaucoma was performed.

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## THE OFF/ON-RATIO OF THE ISOLATED ON-OFF-ELEMENTS IN THE MAMMALIAN EYE

BY

RAGNAR GRANIT

(FROM THE NOBEL INSTITUTE FOR  
NEUROPHYSIOLOGY, STOCKHOLM)

IN this communication I would like to draw attention to some aspects of the micro-electrode work with the retina of the dark adapted decerebrate cat which have come to the fore after the appearance of my (very much delayed) summary in 1947. Some new results and concepts have emerged from the further analysis of several hundred isolated fibres in this retina and it is possible that there is something in this work that may interest the clinician also. It is not my intention to review experiments published elsewhere, except in so far as they are necessary for this discussion of concepts and principles.\*

The retinal elements are either *on-elements*, *off-elements* or *on-off-elements*. The on-elements respond to light with a stream of impulses, the off-elements with a discharge at the cessation of illumination and the on-off-elements combine these two properties. For the discrimination of light and colours the on-off-elements must be the most important ones. In the cat's eye they are also the most numerous ones; there Miss Tansley and I found 80 per cent. on-off-elements. The on-elements turned up in 16 per cent. of our total of 164 elements. We have reasons to believe them to be pure rod-elements. The on-off-elements may differ in colour sensitivity at "on" and "off." For this reason it is impossible to assume that the on and off-components are set up by identical

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\* The original papers will be found in the *Jl. Physiol.*, and *Jl. Neuro-Physiol.*, for 1947. The latest one is due to appear in the latter Journal within a few months. The summary referred to is "Sensory Mechanisms of the Retina," Oxford Univ. Press, 1947.

receptors. Hence the on-off-element is a complex structure to which receptors of different properties have contributed. Some of them must have arrived over internuncial channels involving the retinal synapses. One of the first tasks in retinal physiology is to find out how internuncial activity modifies the primary receptor response. (The latter probably appears in a relatively pure state in the simple on-elements.) For this analytical work it is necessary to develop methods and concepts.

One of the fundamental new concepts is the off/on-ratio. Miss Tansley and I discovered this variation in the properties of the on-off-elements. We increased the strength of the light gradually and found that sometimes the on-, sometimes the off-component of an on-off-element turned up first. An on-off-element is thus relatively more on-sensitive or relatively more off-sensitive. Sometimes the on- and off-components were equally light-sensitive at the threshold and then the off/on-ratio obviously is 1.0. Dr. Gernandt and I have since, independently and together, measured the off/on-ratios for a large number of on/off-elements, stimulating with different wave-lengths. One obtains statistical distribution curves showing that the majority of the elements have off/on-ratios varying from 0.1 to 10.0 but that the extremes of the curve are represented by variations as large as 1000 and 0.001. This, of course, is an amazing variation and one may well ask what purpose it serves.

In a general way one can say that the variation in the off/on-ratios improves discrimination. Most acts of discrimination presuppose a moving eye for which the off-discharge is just as important as the on-discharge. A wide range of variation in the off/on-ratio increases the local variability necessary for discrimination.

In his extensive material Gernandt (unpublished) also has measurements for red ( $0.650 \mu$ ), green ( $0.510 \mu$ ) and blue ( $0.460 \mu$ ) light. Any wave-length may have any off/on-ratio but the probability that the maximum would be in the green was only 0.18 as against 0.39 for the blue and 0.47 for the red light. This means that there are several elements which become relatively more off-sensitive towards either or both ends of the spectrum. Others have a constant off/on-ratio throughout the spectral range. This, of course, is a very interesting finding. My measurements of the spectral sensitivity of dark adapted cats were always carried out with the on-components, when on-off-elements were localized by the micro-electrode. They gave, when averaged, roughly the visual purple distribution of spectral sensitivity (as again confirmed in this laboratory). The off-components (which at present are being measured) cannot do so unless the element is of the type for which

the off/on-ratio is constant throughout the spectral range. Other receptors than those activated by visual purple must therefore contribute relatively more to some off-components. These apparently contain a greater number of cones than the on-components. This conclusion was also reached by Miss Tansley and myself who found that red-sensitivity tended to increase with off-sensitivity.

Another of Gernandt's results was still more interesting. He found, as I had done before, that different on-off-elements are differentially sensitive to adaptation with red, green or blue light. But to this he added the important observation, that, in general, selective adaptation of an on-off-element tended to depress the more sensitive component relatively more, so that if the element was more off-sensitive, the off-component was relatively more depressed and, *vice versa*, if it was more on-sensitive. What this means is best understood with the aid of an example. Assume that the eye be stimulated with a blue stimulus. Then, during illumination, all the specific blue-sensitive on- and off-components become depressed. The off-discharge that follows upon cessation of stimulation will therefore be favoured in off-sensitive elements containing other components than blue ones. This is precisely the kind of arrangement that would facilitate a contrast mechanism operating with on-off-elements.

Let us now consider why the off/on-ratio varies as it does. The fact itself seems rather remarkable. All receptors are working at their maximum capacity because the eye is fully dark adapted. How then is it possible for some to be a 1,000 times less sensitive than others? The on-component may be 1,000 times more sensitive than the off-component and, *vice versa*, the off-component 1,000 times more sensitive than the on-component. The off/on-ratio may thus vary from 1000 to 0.001. This occurs despite the fact that hardly any elements are likely to be *pure* cone-elements. There is always a great deal of convergence of rods and cones towards the ganglion cell from which the micro-electrode picks up the response. The rods will dominate in dark adaptation.

Nevertheless the assumption that the variation in the off/on-ratio really expresses a variation in the cone/rod-ratio deserves to be examined. If true it would mean that the less sensitive component is dominated by cones. Thus, when the off/on-ratio is high, the on-component would contain the cones, when the off/on-ratio is low the cones would be in the off-component. Available evidence does not support this simple explanation. On the contrary, the higher the off/on-ratio, the greater, on an average, the relative sensitivity to red light ( $0.650\mu$ ) for both the on- and the off-component. This was found by Miss Tansley and myself

with 61 on/off-elements. At the wave-length  $0.650\mu$  the photo-sensitivity of visual purple is of the order of 0.3 per cent. of its maximum around  $0.500\mu$  so that a positive correlation between off/on-ratio and red-sensitivity can only mean that the higher the off/on-ratio the more likely that cones participate in the response.

There is another very potent argument against the idea that the off/on-ratio would be a variable illustrating merely the relative contribution of cones to the on- and off-components of the elements. This presupposes that the off/on-ratio would be constant but actually it is only constant just at the threshold and, above it, and is subject to great fluctuations under the influence of light-stimuli. Electrical stimulation of the eye also changes the off/on-ratio at the threshold. Now this is not surprising. Stimulation with light produces differences of electrical potential across the retina so that if this influences the off/on-ratio, direct electrical stimulation must do so too. The curves illustrating impulse frequency against stimulus intensity also demonstrate variations in the off/on-ratio. Sometimes the on-effect is inhibited within a certain range of intensity, sometimes the off-effect (Granit, *Jl. Physiol.*, 1944, Vol. CIII, p.103). Impulse frequency is by no means a simple function of stimulus intensity when one records from a single fibre *after* the effect has passed through a nervous centre. The optic nerve, of course, is really a central tract and this accounts for the difficulties in interpreting the message. It has already become highly differentiated. The frequency-intensity function has become modulated in the retinal centre.

With these facts at our disposal we can readily understand that the variation in the off/on-ratio at the threshold represents the selection of one particular state of balance between the forces of excitation and inhibition (or suppression) in the retina. This conclusion leads to the novel and somewhat radical concept that an element, already at the absolute threshold, is subject to "internal tension" exerted by forces of facilitation and depression. The synaptic organization maintaining the element in a resting retina (at the absolute threshold) cannot be regarded merely as an anatomical distribution pattern of the paths of various receptors, bipolars, amacrine and horizontals but it is also a structure using energy in order to suppress the activity of certain cells and, perhaps, heighten that of others. The threshold variations in the off/on-ratio demonstrate how this semi-stationary state of balance of forces within an on-off-element is organized at one particular level of intensity.

It would not surprise me if the extremes represented less probable labile states. I have seen several on-off-elements with off/on-ratios of the order of 0.001 under the influence of electrical

polarization acquire an off/on-ratio of around 1.0. This change has been in the nature of a release of the suppressed component under the influence of the electrical stimulus. The latter has been delivered from electrodes on opposite sides of the bulb.

Long ago Dr. L. A. Riddell and I myself (*Jl. Physiol.*, 1934, Vol. LXXXI, p. 1) noted with the frog's eye that a light adapted retina was a relatively more negative retina (inside more negative to outside of bulb) and pointed out that light adaptation involved slow electrical changes altering the "state" of the retina. In a later summary I spoke of "electro-adaptation." It will now be necessary to return to similar problems with the mammalian eye.

It is highly probable that the slow electrical changes induced by light determine the off/on-ratio because electrical stimulation strongly affects this relationship. But recent observations from experiments now in progress have led me to suspect that we are allowing ourselves to be too dogmatic when tacitly assuming that the anatomical organization is fixed and unchangeable. I believe that we must seriously consider the possibility that the "boutons" at the synapses expand or contract so as to alter the contact surface. In certain types of on/off-elements I find that stimulation with light induces large changes of electrical threshold. These often return very slowly and sometimes the responses to anodal and cathodal currents and those to illumination at "on" and "off," shift relative to one another in such a manner that one must raise the question as to whether one really is dealing with the same anatomical organization.

On the whole I feel that one should not be afraid of putting radical views to the test of an experiment. It seems to me a greater mistake to assume that a new technique, such as the micro-electrode technique, must necessarily answer questions suggested by the very different psychophysical method of approach. If we frame our questions on the basis of old findings the new technique may refuse to answer them. Our aim must be to put the right questions to the micro-electrode.

THE PRESENT POSITION OF THE PROBLEM OF  
THE INTRA-OCULAR FLUID AND PRESSURE

BY

SIR STEWART DUKE-ELDER *and* H. DAVSON*From the Department of Physiology, University College, London*

ALMOST half a century ago when Parsons was working on the problem of the intra-ocular pressure, a change in the conception of the nature of the aqueous humour was emerging. Previously—without firm experimental evidence—the aqueous was generally accepted as being a secretion: it was of “vital” origin and in an age of dogma it was accepted as such. With the growth of the mechanistic conception of biology which characterised the end of the last century, however, and stimulated particularly by Starling’s work on the body-fluids generally, Parsons, in conjunction with Henderson and Starling in England, concluded that the aqueous, like the tissue-fluids elsewhere, was a simple filtrate governed by hydrostatic and osmotic forces. A quarter of a century later advances in experimental technique, particularly in the physico-chemical approach to biological problems, made it clear that a conception so simple would not suffice. The chemistry of the aqueous was found to be incompatible with such an origin, and a new theory was introduced that this fluid was a dialysate in thermo-dynamical equilibrium with the blood and that upon it a through-and-through circulation was superimposed by pressure-differences at two points of its most intimate association with the blood—the ciliary capillaries and Schlemm’s canal.

Such a theory has very special requirements:—

(a) The intra-ocular pressure (I.O.P.) should be determined by the mean level of the capillary pressure (C.P.) less the colloid osmotic pressure of the plasma proteins (O.P.), *i.e.*, by the relationship:

$$\text{C.P.} - \text{O.P.} = \text{I.O.P.}$$

With an average value of 20 to 25 mm. Hg for the intra-ocular pressure and a figure of 28 mm. Hg for the colloid osmotic pressure of the plasma proteins, the theory therefore demands a mean level of capillary pressure of about 50 mm. Hg. As a corollary to this relationship a rise in the level of capillary pressure should be reflected in a rise in intra-ocular pressure, whilst a rise in the colloid osmotic pressure of the plasma should lower the intra-ocular pressure.

(b) A fluid formed by filtration from the blood plasma and retained for some length of time in the chambers of the eye is not only an ultra-filtrate but a dialysate, *i.e.*, it has had time to

come into thermodynamic equilibrium with its parent plasma supposing that this equilibrium had not been established at the moment of filtration. The Gibbs-Donnan equilibrium should therefore apply to the aqueous humour and plasma: this requires that the concentrations (or activities) of all non-electrolytes capable of penetrating from the plasma into the aqueous humour be equal in the two fluids. The following relationship should apply to the distribution of the univalent ions:—

$$\frac{[\text{Concent. of Na in Plasma}]}{[\text{Concent. of Na in Aqueous}]} = \frac{[\text{Concent. of Cl in Aqueous}]}{[\text{Concent. of Cl in Plasma}]}$$

From this it follows that the osmotic pressure of the plasma should be greater than that of the aqueous humour.

(c) A rise in the concentration of one of the constituents of the blood, (*e.g.*, sugar), or the introduction of a diffusible foreign substance into the blood should be followed by diffusion of the substance in question into the aqueous humour in accordance with Fick's Law, *i.e.*, at a rate proportional to the difference in the concentrations in the two fluids. The relative rates at which various substances enter the eye under these circumstances would be a characteristic of the "Blood-Aqueous Barrier." It should be noted that the complete impermeability of the barrier to certain substances is not inconsistent with the dialysis theory.

These are the main demands of the theory and we have indicated that fifteen years ago there was no serious discrepancy between theory and experimental fact. The same evolution, however, has repeated itself in scientific progress. Further factual experimental results obtained by more exact and elaborate techniques have appeared: these have again rendered a relatively simple and apparently satisfactory theory inadequate. And when any theory—no matter how simple and satisfying—fails to accommodate new facts determined by newer and better methods of experimentation, the theory—no matter how useful it may have appeared—must be sacrificed. Just as Newton's Theory of Gravitation gave place to Einstein's Theory of Relativity, so the theory of dialysation must give place to something else. Unfortunately the phase of transition from one conception to another is usually a period of some confusion, and for this reason it may be of value to assess the present position and to indicate the possible direction of progress.

#### EXPERIMENTAL FINDINGS

Some experimental facts will now be recapitulated.

I. *The Distribution of Sodium and Chloride.*—Van Slyke calculated that the ratio ( $R_{Na}$ )—concentration of Na in plasma/concentration in a dialysate—should be 1.04, the corresponding ratio

for chloride ( $R_{Cl}$ ) being 0.96. Recent studies from this laboratory (Davson, Duke-Elder and Benhami, 1936; Davson, 1939; Davson and Weld, 1941; Hodgson, 1938) have partly confirmed and partly disproved the existence of a Donnan equilibrium in this regard. Thus in cats the value of  $R_{Na}$  is  $1.03 \pm 0.004$ ;  $R_{Cl}$  is 0.945. In the dog  $R_{Na}$   $1.04 \pm 0.004$ , i.e., it agrees exactly with Van Slyke's theoretical requirement.  $R_{Cl}$ , however, is grossly aberrant, being on the average 0.92, extreme values as low as 0.89 having been observed. Chloride is thus not in equilibrium with the blood plasma, its concentration in the aqueous humour being too high. The position, however, is complicated by the fact that recent studies on dialysis with collodion membranes indicates that Van Slyke's theoretical ratios may be wrong. Greene and Power (1931) and Ingraham, Lombard and Visscher (1933), for example, obtained results which indicate that  $R_{Na}$  should be nearer 1.08 than 1.04 and that  $R_{Cl}$  should be in the region of 0.99 rather than 0.96. If this is true the observed values of  $R_{Na}$ , namely 1.03 in the cat and 1.04 in the dog, are no evidence for equilibrium but rather of the existence of an excess of sodium in the aqueous; similarly the observed value of  $R_{Cl}$  of 0.945 and 0.92 indicate an excess of chloride in the intra-ocular fluid. By dialysing aqueous humour against plasma from the same animal it has been shown in our laboratory (Davson, Duke-Elder and Maurice, 1948) that sodium and chloride do actually migrate from aqueous humour to plasma to give final equilibrium ratios of 1.06 to 1.07 for sodium and 0.98–0.99 for chloride. There is thus no doubt that the sodium and chloride of the aqueous are not in thermodynamic equilibrium with these substances in the plasma.

Here, however, we are not certain that all the circumstances have been taken into consideration. Thus it is known that the aqueous contains a higher concentration of lactic acid than the blood of the jugular vein (an excess of 1.7 millimoles per litre, Fischer, 1931), due, presumably, to the formation of this substance as a metabolite by the lens and retina. Some part of the excess of sodium in the aqueous might be fairly accounted for by its combination with lactic acid (1.7 out of a total excess of about 3.0 millimoles per litre): the remaining moiety is not accounted for—nor can the excess of chloride be explained on a similar basis, and since it persists in the aphakic eye any metabolic influence of the lens must be ruled out. Some activity in respect of sodium and chloride other than dialysis must therefore exist.

A further complicating factor is the entrance of sodium and chloride into the posterior segment of the eye. It has been shown from this laboratory (Davson, Duke-Elder, Maurice, Ross and Wooden: in press), by the use of tracer elements, that sodium



(and potassium) do not penetrate into the vitreous chamber from all the vascularised tissues as do substances like glucose and thiocyanate, but enter essentially through the ciliary region. In this, as we shall see in a moment, there is an analogy with the cerebral circulation; but from the point of view of the immediate argument, this fact reinforces the argument for a special mechanism for the transference of these substances through the blood-aqueous barrier and localises it (largely, at any rate) to the ciliary region. Not only must we therefore postulate some mechanism of transfer for electrolytes differing quantitatively from simple ultra-filtration or dialysis, but we must also admit the existence of qualitative regional differences in the operation of this mechanism.

II. *Reducing Substances: Carbohydrates.*—The distribution of sugars is somewhat simpler. If the concentration of reducing substances (glucose) in the aqueous is estimated it is found to be lower than that in the plasma, while that in the vitreous is lower still. In the cat, for example, the relative values have been found in this laboratory to be: arterial plasma 108, aqueous 82.5, vitreous 57 (Davson and Duke-Elder, 1948; see also Adler, 1930). Regarded superficially it might be said that a theory of simple dialysis requires these values to be equal; but the deficiency in the aqueous is approximately equal to the glucose uptake of the lens, and that in the vitreous to the metabolic requirements of this tissue and the retina. That this explanation actually accounts for the deficiency is suggested by the fact that it largely disappears, so far as the aqueous is concerned, in the aphakic eye (when the concentration of sugar in the aqueous approximates that in the plasma), and becomes very much greater in the posterior segment if an excised eye is incubated so that the retinal metabolism is maintained and the alternative sugar supply by the blood cut off (when the retina will consume more sugar) (Davson and Duke-Elder, 1948). It is interesting that the concentration of glucose in the cerebrospinal fluid is very low, about the same as that in the vitreous body: in the brain conditions are very similar to those in the posterior segment of the eye.

Moreover, a study of the kinetics of the entry of carbohydrates into the eye has shown that this class of substance passes the blood-aqueous barrier at relative speeds which suggest a simple physical diffusion depending on the size of the molecules concerned (Davson and Duke-Elder, 1948). Thus pentoses (xylose) and hexoses enter the aqueous at about the same rate, disaccharides (sucrose) at a rate about one-seventh of this and polysaccharides (raffinose, inulin) at a barely measurable rate. This would suggest a simple diffusion through pores of a limiting size slightly larger than the molecules of sucrose; and the fact that natural sugars (glucose) enter at the same rate as synthetic sugars of comparable

molecular size (3-methyl-glucose, which is not phosphorylated *in vivo*) would seem to preclude any secretory mechanism so far as this type of substance is concerned. Into the vitreous body the rate of entrance is much slower, suggesting a quantitative difference in the posterior segment of the eye; and the fact that pentoses and hexoses enter at somewhat different rates into the vitreous body may indicate the presence in this region of a qualitatively different mechanism which can exert a chemical as well as a physical differentiation.

III. *Nitrogenous Substances*.—The case of nitrogenous substances is peculiar. As long ago as 1933 Adler drew attention to the fact that the concentration of urea in the aqueous humour was definitely below that in the plasma: according to his figures the concentrations in aqueous and plasma in the cat are 46.3 : 54.9; that is, there is a difference of 0.0014 M. The subject has been investigated in greater detail subsequently in Adler's laboratory as well as in ours and at Boston (Adler, 1933; Kinsey and Grant, 1942; Benham, 1937; Scheie, Moore and Adler, 1943-7; Kinsey and Robinson, 1946; Ross, unpublished). The observed ratio depends in a considerable measure on the chemical methods of estimation; thus Kinsey and his co-workers claimed one ratio only to alter it as a result of applying another chemical method: with a conductivity method Benham from this laboratory obtained a ratio of 0.8 to 0.95 in the rabbit and 0.9 to 0.95 in the cat: whilst with the Conway method, Ross, working in our laboratory, has recently obtained a ratio in the cat of 0.81. There is no doubt, however, that urea is present in lower concentration in the aqueous humour than in the blood plasma. Accurate studies of other organic compounds such as amino-acids and creatinine have not been reported and would probably mean little owing to the unspecificity of the chemical methods employed: what evidence we have obtained in recent permeability studies suggests that there is a deficiency of these compounds in the aqueous humour. Again, this deficiency cannot be explained by a theory of dialysis; nor can metabolic consumption provide a reason for the discrepancy. It has been found in this laboratory, however, that not only urea but all nitrogenous substances such as creatinine, and amino acids as glycine and alanine with their relatively small molecules penetrate the blood-aqueous barrier very slowly and with difficulty (at about 1/3 the rate of the large-molecule sugars) (Davson Duke-Elder, Maurice, Ross and Woodin, *in press*). It is obvious that if there is a relatively easy exit from the eye by fluid in bulk and a preferentially difficult entrance of these substances, they may for purely physical reasons be in constant deficit in the "steady-state" of normal conditions (Kinsey and Grant, 1942-4; Duke-Elder and Davson, 1943; Bárány and Davson, 1948).

It is interesting that sucrose injected into the blood stream tends to distribute itself between aqueous humour and plasma so that at equilibrium its concentration in the aqueous humour is only about half that in the plasma (unpublished). Sucrose penetrates from blood to aqueous humour very slowly indeed, much more slowly than even urea, and should, by the same explanation, have a distribution at equilibrium at the "steady-state" such that the ratio of the concentrations in aqueous humour and plasma is smaller than that for urea; this has, in fact, been found (unpublished). The finding of a deficiency of a substance in the aqueous humour is no evidence of itself in favour of a secretory origin of this fluid, as has been argued (Adler, 1933).

It has been known for some time that the concentration of ascorbic acid (vitamin C) in the intra-ocular fluid is considerably greater than that in the blood plasma: this difference is much more marked in some animals (e.g., rabbit and ox) than in others (e.g., the cat and dog). There are at present two schools of thought as to the cause of this excess of ascorbic acid: Müller and Buschke (1934) showed that in the aphakic eye the difference in concentration was very considerably less and brought forward evidence purporting to prove that the lens actually synthesised the vitamin (Müller, 1935). Friedenwald, Buschke and Michel (1943), on the other hand, regard the high concentration as evidence of secretion by the ciliary body and in a recent study Kinsey (1947) certainly supported this hypothesis by showing that ascorbic acid, injected into the blood, passed into the aqueous humour in spite of the fact that the concentration was higher than in the plasma. If, however, the lens synthesised ascorbic acid, it would continuously pass into the aqueous humour and thence into the blood stream by simple diffusion: increasing the blood concentration would lower the rate of loss from the aqueous humour and thus allow the ascorbic acid concentration to pile up to a greater extent. The matter clearly merits further investigation.

IV. *Osmotic Pressure.*—Our early studies on the osmotic pressures of the aqueous humour and plasma (Benham, Davson and Duke-Elder, 1937) indicated that there was an excess of osmotic pressure in the plasma as compared with the aqueous so that the requirements of the dialysis theory appeared to be met. More recent work from the same laboratory (Benham, Duke-Elder and Hodgson, 1938), however, has shown that when ether anaesthesia, which raises the osmotic pressure of the plasma, was avoided, the osmotic pressure of the aqueous humour was always greater than that of the plasma, a difference in osmotic pressure in the opposite sense from that required by the Donnan equilibrium. This finding has been confirmed by Røepke and Hetherington (1940) who have shown also that the excess of osmotic pressure in the aqueous humour could be abolished by poisoning the eye with an intra-ocular injection of mercuric chloride. The finding that when aqueous humour is dialysed against plasma there is a decrease in conductivity of the former fluid (Davson, Duke-Elder and Maurice, 1948) corroborates these later findings and indicates that the excess of osmotic pressure is at least in part due to an excess of electrolyte in the aqueous humour. Analyses of the concentrations of non-electrolytes certainly indicate that they are unable to contribute to an excess of osmotic pressure in the aqueous humour; in fact, they must cause a material deficiency. A rough estimate indicates that the deficiency of sugar, urea, creatinine, amino-acids and protein

would amount to about 4.5 millimoles per litre; consequently, if the osmotic pressure of the aqueous humour is to be actually greater than that of plasma, an excess of at least some 4.5 millimoles of some other material, presumably salt, would be necessary. The dialysis experiments described above indicate that the concentration of sodium in the aqueous humour is about two per cent. higher than the equilibrium concentration, *i.e.*, there is an "excess" of about 3.0 millimoles per litre. The excess sodium ions must, of course, be accompanied by negative ions and if these are monovalent (*e.g.*, chloride) this would demand a further 3 millimoles per litre. The excess sodium in the aqueous humour can thus fully account for the deficiencies of organic substances such as sugar and urea, in fact, it is sufficient to reverse the osmotic relationships between a dialysate and plasma causing the osmotic pressure of the aqueous humour to be the greater. It may be that the maintenance of this osmotic gradient is of considerable importance in the mechanism of the intra-ocular pressure.

V. *The Intra-ocular Pressure.*—It has frequently been said that the absence of an invariable and proportional variation in the intra-ocular pressure in response to changes either in the blood pressure or the colloid osmotic difference between plasma and aqueous is incompatible with a dialysation theory. The classical researches of Parsons (1904—8) and Henderson and Starling (1904) have shown that the intra-ocular pressure does indeed follow the arterial in sudden changes in experimental animals; the more recent work of Duke-Elder (1926—30) has confirmed this. This, however, applies only to dramatic experimental changes. It must be remembered that the intra-ocular pressure will vary with the capillary pressure. It has not been possible to measure the capillary pressure directly in experimental investigations of this problem and one has had to assume that a rise in arterial pressure would be reflected in a rise in capillary pressure, but it would be rash to say what fraction of the rise would correspond to a rise in capillary pressure, or that the rise is in all circumstances proportionately the same. Duke-Elder found in general that the rise in intra-ocular pressure in experimental animals was about one-tenth of the rise in arterial pressure, but outside the experimental environment this relationship probably does not hold. It would seem that, teleologically speaking, the vascular system is designed to provide a reasonable constancy of capillary pressure; changes in the calibre of the arterioles may produce changes in the peripheral resistance so that a rise in arterial pressure could be largely compensated and the capillary pressure remain comparatively unchanged.

Recently Bárány (1946—7) has shown that unilateral closure of

the carotid artery in the rabbit causes a fall in intra-ocular pressure associated with a fall in arterial pressure; after a time, however, the intra-ocular pressure returns to normal although the arterial pressure remains permanently depressed in the ear of the operated side. Bárány's results seem to show that the intra-ocular pressure does, indeed, respond to a sudden change in arterial pressure, but that there is some compensatory mechanism at work which eventually keeps the intra-ocular pressure independent of the arterial. Bárány has argued that the response of the eye to a change in arterial pressure is not by any means as large as might be expected on the basis of the dialysis theory if it is assumed that the capillary pressure remains a constant fraction of the arterio-venous difference. This assumption, however, requires justification.

The influence of the colloid osmotic pressure of the plasma on the intra-ocular pressure may, as we have seen, be deduced from the simple equation already stated: a decrease in the former should raise the latter and *vice versa*. In experimental animals these deductions have been borne out qualitatively. Dilution of the plasma with isotonic saline undoubtedly causes in experimental animals a considerable rise in intra-ocular pressure (Duke-Elder, 1931); it is difficult to increase the colloid osmotic pressure of the plasma by injections of gum acacia; Bárány (1947) has recently suggested that the earlier results of Duke-Elder (1931) may have been a factitious result of the toxicity of the gum acacia rather than a true osmotic effect. The decrease in intra-ocular pressure following a massive injection of hypertonic NaCl or sucrose belongs to the same category of osmotic effects; temporarily the osmotic pressure of the blood is raised in comparison with that of the aqueous humour and water is withdrawn from the eye by osmosis. If the high osmotic pressure of the plasma were maintained for some time, as in experimental animals, the extra NaCl or sucrose would diffuse into the eye and so tend to lower the osmotic pressure difference, and eventually the intra-ocular pressure would tend to return to normal. The effects of long-continued maintenance of an abnormal colloid osmotic pressure of the plasma may be observed in man in nephritis: Robertson (1939) has emphasised that there is no coincidental rise in the intra-ocular pressure in this condition and has made this the basis for the claim that the aqueous humour is formed as a pure secretion. His conclusions indicate the existence of some compensatory mechanism whereby slowly developing and long maintained changes in the osmotic pressure of the plasma may be neutralised in so far as the intra-ocular pressure is concerned.

This compensatory mechanism is at present unknown; but we may suppose it may involve two components, one vascular and

the other concerned with drainage of fluid from the eye. The presence of local axon reflexes exerting a powerful influence on the ocular circulation has been demonstrated (Duke-Elder, 1931); the eye is the only organ in the body wherein these have been found and in their presence is surely of significance. Moreover, the presence of a central mechanism (? hypothalamic) maintaining the control of the tonus of the eye at a relatively constant value would merely bring this into line with practically all physiological functions. About this at present we know nothing; but many facts regarding the tension of the eye and the interdependence of the tensions of the two eyes suggest its presence.

VI. *The circulation of the intra-ocular fluid.*—The evidence in favour of a continuous drainage from the eye is largely clinical, depending on the occurrence of iris bombé and the effects of denying access of the fluid to the angle of the anterior chamber. There have been several attempts to measure the rate of drainage or flow in experimental animals. Thus Troncoso (1921) measured the dilution of the blood in the anterior ciliary veins, and, on the assumption that this dilution was due to a bulk reabsorption of aqueous humour, computed that the rate of drainage was about 2 to 3 cu. mm. per min. Friedenwald and Pierce (1932) replaced the aqueous humour with plasma in an attempt to block the drainage route completely; they then measured the rate of inflow into the eye and argued that this was the normal flow. This method is open to some very serious objections, principally owing to the radical disturbance of the difference in colloid osmotic pressure between the two fluids. He obtained a flow-rate of 1 cu. mm. per min. in the dog. Kinsey and Grant (1942) computed a value of 4 cu. mm. per min. in the rabbit from the observed rate of penetration of radioactive sodium but the computation rests on assumptions that have not been proved and are difficult to justify in the light of our present knowledge. There has thus been no definite proof of a bulk *non-selective* drainage from the anterior chamber of experimental animals; but this has been provided recently in our laboratory (Davson, Duke-Elder and Maurice, unpublished). The principle adopted was to replace (under suitably controlled conditions) the aqueous of the cat by an artificial aqueous humour containing about 100 mg. per 100 c.c. of inulin (a large molecular weight substance that could only leave the eye by a non-selective drainage route: diffusion through the blood-aqueous barrier would be out of the question). Throughout the experiment the concentration of inulin was maintained at a higher level in the blood than it was in the artificial aqueous humour; any loss of inulin from the eye must therefore have been due to a bulk-flow mechanism since diffusion through the blood-aqueous barrier (assuming this to have been made sufficiently abnormal by the

experimental technique to permit the passage of inulin) could only occur from blood into the eye. After an interval of fifteen minutes or half an hour the "aqueous humour" was withdrawn and submitted to analysis. The results proved that inulin may be drained away from the eye and represent the first unequivocal proof of drainage in bulk.

It is obvious that the composition of the aqueous humour will be materially altered by this drainage; and it is equally obvious that it will upset any assumptions regarding the height of the intra-ocular pressure based on the formation of the intra-ocular fluid alone. The position is rendered still more complicated by the demonstration of aqueous veins by Ascher (1942—4) supplementing the original conception of drainage through the canal of Schlemm alone. It is interesting that Friedenwald and Pierce (1932) brought forward evidence to show that the capacity of drainage increased five to ten times if the intra-ocular pressure were raised a few mm. Hg above its normal level. Further consideration, both theoretical and experimental, on the influence of capillary and osmotic pressure on this mechanism will certainly produce results of more than usual interest.

#### DISCUSSION

From the above short recapitulation of experimental facts it is obvious that the intra-ocular fluid cannot be a simple dialysate in equilibrium with the capillary plasma. It is true that the metabolism of the sugars is largely compatible with such a theory—simple dialysis through the jellyish cement substance occupying the intercellular spaces in the capillary endothelium and epithelial membranes, the watery spaces of which act as pores. A study of nitrogenous substances, however, completely upsets this view-point; urea penetrates more slowly than glucose although it has much the smaller molecule; the same is true for creatinine and more so for amino-acids. Penicillin is smaller than sucrose yet its rate of penetration is very slow indeed, about one fifth of that of sucrose. Evidently the presence of the nitrogen atom in the molecule slows down the rate of penetration, in comparison with a molecule of the same size without nitrogen; this is tantamount to saying that the chemical composition of a substance is more important as a determinant of rate of penetration of the barrier than its molecular size. From this it may be concluded that some substances at least must penetrate by way of the cells; the interstitial spaces could not select molecules on the basis of their structure, such selection being a characteristic of the envelopes of individual cells. A striking instance of the importance of chemical structure in penetration is shown by the observation of

Palm (1947) that ethyl alcohol penetrates very rapidly into the aqueous humour, some five to six times as fast as glucose; undoubtedly this is because of the high fat solubility of ethyl alcohol which permits it to diffuse rapidly through cellular membranes. Moreover, the excess of electrolytes with the consequent excess of osmotic pressure of the intra-ocular fluid suggests that some cellular activity is in question. Studies of the most varied nature in other organs of the body have consistently failed to produce any evidence that the capillary wall acts otherwise than as a simple filter; it may block substances, but it has not, so far, been detected in the act of secreting any substance (Landis, 1946). The presumption is, therefore, that any cellular activity is localised in the lining epithelium of the eye (presumably mainly in the ciliary region).

The second general point which emerges is that not only is the mechanism more complicated than dialysis since it differentiates between substances on a chemical basis, but the blood-aqueous barrier differs radically in different localities of the globe. In general, when a given substance penetrates into the aqueous humour it also penetrates the vitreous body more slowly. We have seen that in the most simple case—that of sugars—entrance into the anterior chamber (through the iris) is easy and undifferentiated except in respect to the physical size of the molecules: entrance into the vitreous, on the other hand, is slower and shows some chemical discrimination. By freezing the eye suddenly during the diffusion process it may be shown that certain substances enter the vitreous body predominantly by way of the ciliary body and diffuse backwards towards the posterior pole; other substances, however, can apparently enter the vitreous body rapidly from all parts of its periphery (Davson and Duke-Elder, 1948; Davson, Duke-Elder, Maurice, Ross and Woodin, in press). Sodium and potassium are two instances of substances the route of which to the vitreous body is largely confined to penetration from the ciliary region; glucose and thiocyanate, on the other hand, are examples of substances that can diffuse from the choroidal and retinal circulations. This is a remarkable finding and brings out the strong analogy, if not the identity, between the capillaries of the cerebral and retinal vascular systems. It has been recognised for some time that the capillaries of the cerebral system are radically different from those in other parts of the body. Palm (1947) has recently shown that, alone of the capillaries of the body, those of the central nervous system and the retina do not take up certain acid dyes (trypan blue). On the other hand, Friedenwald and Stiehler (1938) found that acid dyes penetrated the ciliary capillaries with ease. In the rest of the body the



capillaries show no power of differentiating between such substances as urea and sugar and it is generally accepted that diffusion through the walls of these capillaries is a matter of diffusion through quite large intercellular spaces, spaces that are large enough to allow the molecule of inulin, for example, to pass through. The capillaries of the cerebral system, on the other hand, seem to allow sugar and various monovalent ions to penetrate into their surrounding interstitial or perivascular spaces at much slower rates, and they also show some selectivity. If the retinal vessels were similar to those in the muscles, for example, we should expect glucose, sucrose, raffinose and even inulin to penetrate rapidly into the vitreous body, and the fact that penetration of these substances, when it does occur, is less rapid than that into the aqueous humour indicates the highly selective character of the retinal capillaries. The vitreous body, of course, comes into relation with the capillaries of the uveal system—the capillaries of the choroid and ciliary body; here, however, it is separated by membranes and cellular structures from these capillaries and their interstitial fluid (the epithelium of the ciliary body and the whole of the retina including the pigment epithelium). It might be presumed that these structures could impart some selectivity to this part of the barrier separating the vitreous body from the uveal blood plasma.

Although the simple dialysis theory appears to be wrong, as the most recent work from our laboratory (among others) has shown, nevertheless the fairly close similarities in chemical composition of aqueous humour and plasma, together with the partial conformity of the intra-ocular pressure to changes of osmotic pressure and capillary pressure indicate that the simple physical factors of diffusion and osmosis are operative. Can these apparently contradictory findings be reconciled? At the moment there seem to us to be two general possibilities. First we may consider in detail an idea adumbrated from this laboratory ten years ago (Duke-Elder, 1938); on this basis the aqueous humour is formed primarily as an ultra-filtrate of plasma and, superimposed on this simple process, there is some activity which modifies the concentrations of certain substances, notably sodium and chloride, in the aqueous humour, giving certain peculiarities including an excess of osmotic pressure to this fluid. It is well recognised that the permeability of membranes is influenced by differences in the surface electrical charges and in the hydrophilic swelling of the proteins on either side of the membrane so that some degree of uni-directional permeability and the capacity for maintaining concentration gradients exist. Such a complex membrane offers itself in the ciliary epithelium, and the work of Friedenwald and Stiehler (1938) suggests a possible mechanism. They suppose that the energy

necessary for such modifications depends upon a difference of potential maintained between the ciliary stroma and epithelium by oxidative and reductive processes owing to the presence of Warburg's respiratory enzyme in the latter. It is true that these conclusions are based on the intra-vital action of dyes—a very confused and difficult problem susceptible to several explanations; but the possibility of some such activity cannot be ruled out of court. Further exploration along these lines would be of great interest.

If we assume such an activity on the part of the ciliary epithelium, as a result of this excess of pressure the driving pressure of fluid into the eye consists of the whole of the capillary pressure (instead of the capillary pressure *minus* the colloid osmotic pressure of the plasma) *plus* an excess of osmotic pressure. Fluid is thus forced into the cavities of the eye with an available pressure-head of from 50 to 75 mm. Hg. Since there is no counter-pressure the intra-ocular pressure must equal this driving pressure unless there is a leakage of fluid out of the eye; the intra-ocular pressure is in effect 25 mm. Hg so that there must, in this view, be a rapid drainage of fluid out of the eye. This outflow would therefore be of maximal importance in the mechanics of the ocular tension, and blockage of the drainage routes must, on this basis, result in a serious rise in intra-ocular pressure since the normal intra-ocular pressure is maintained at its low level only as a result of leakage.

An alternative theory that must also be borne in mind when considering the experimental data is the following:— The aqueous humour may be elaborated entirely within the cells of the ciliary epithelium and possibly to a less degree in other cellular linings of the eye. The fluid so formed is extruded into the posterior chamber of the eye as a "primary aqueous humour"; as a pure secretion it may have characteristics entirely different from those of the blood. The fluid so formed would be forced into the posterior chamber with a certain secretion pressure; if drainage occurred at the angle of the anterior chamber this forcing of fluid into the eye would result in a flow through the pupil. The primary aqueous humour on its passage out of the eye would not, however, be insulated from the blood plasma, but would be in communication with it through the iris and, through the medium of tissue-fluid, through the intercellular spaces of all the lining membranes; it would thus tend to attain diffusion equilibrium with the blood. If diffusion equilibrium were completely attained the result would be that the aqueous humour would appear to be a simple dialysate in spite of its secretory origin. It can be postulated, however, that the aqueous humour does not remain in the eye long enough for

this diffusion equilibrium to be established, so that an intermediate state is achieved in which it has strong characteristics of a dialysate but betrays its secretory origin in important details, such as an osmotic pressure greater than that of the plasma, a higher concentration of sodium and chloride than required of a dialysate, a low concentration of urea, a high concentration of ascorbic acid, and so on. On the basis of this theory most substances must enter the eye by a cellular route whereas on the modified dialysis theory discussed above, much of the fluid formation could have been by way of the intercellular spaces only, the osmotic excess of material being added by the cellular activity of the lining membrane. On the experimental evidence, however, this hypothesis would seem unlikely.

Such are two tentative suggestions. Others may offer themselves, but it is obvious that in the present state of factual knowledge no pragmatic conclusion can be reached. The problems presented are full of interest and are not without their difficulties; their solution must await the results of more extensive and detailed experimental work.

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## PARTICIPATION OF THE OCULAR APPENDAGES IN SYMPATHETIC OPHTHALMIA AND ITS BEARING ON ENUCLEATION

BY

BERNARD SAMUELS

NEW YORK

THE special incentive for this paper is my conviction that not infrequently following the enucleation of the exciting eye in sympathetic ophthalmia a considerable amount of inflamed tissue is left in the orbit. Sufficient emphasis does not seem to be placed on the fact that although sympathetic ophthalmia is primarily a disease of the inner eye yet the appendages may also be involved simultaneously.

### NATURE OF SYMPATHETIC OPHTHALMIA

Histologically sympathetic ophthalmia declares itself in the guise of an infiltration of lymphocytes, epithelioid cells and giant cells in the uveal tract of each eye. The peculiarity lies not so much in the elements of the infiltration, which are similar to those of tuberculosis, but rather in the selective affinity that the disease exhibits for uveal tissue. A characteristic feature of the disease is the tendency of the infiltration to expand outward beyond the globe. Inwardly, any involvement of the pigment epithelium and retina is invariably so slight as to be of no real consequence. Nor is the choriocapillaris attacked, apparently because the interspace between the capillaries is composed of tissue that is not typically uveal and therefore is not suitable soil.

## CAUSE OF SYMPATHETIC OPHTHALMIA

As far back as 1905 Parsons, in his *Pathology of the Eye* expressed his opinion that sympathetic ophthalmia "is an endogenous infection by ultraviolet organisms." The accumulated evidence of countless histological examinations of the exciting eye has served to strengthen this theory. Certainly the inflammatory reaction of the tissues attacked presents all the earmarks of a non-pyogenic infection. The most mysterious aspect of the disease is the fact that the virus supposed to be responsible has never been isolated or seen. In any event, the very essence of sympathetic ophthalmia is a perforating wound in one globe through which the virus may enter.

## PATHWAYS OF THE VIRUS AS REVEALED BY INFLAMMATORY REACTION (OMITTING MANY MINUTIAE)

A. *Pathway along the uveal tract.* Perforations in the region of the ciliary body, which, to borrow a term from Nettleship, is called "the dangerous zone," are the most feared because they are apt to be accompanied by prolapse of the iris and ciliary body, either one of which forms a favourable point from which the virus may travel into the interior of the eye. When the opening is large, the blood supply to the prolapse being little impaired and the part being released from intra-ocular pressure, the reaction may be so great as to attain tumour-like proportions and resemble a staphyloma (Fig. 1). On the other hand, there may be little or no reaction at or near the opening; for with the globe as with any other part of the body, it is possible for bacteria to enter without causing a primary lesion. The advance of the virus posteriorly may be blocked completely by a zone chorioretinitis produced by traction on the part of a detached retina. Such confinement of the infiltration to the area near the perforation is a most striking anatomical proof of the extra-ocular origin of the virus (Fig. 2).

The development of the infection in the choroid may be divided into two stages. (1) The appearance of small lymphocytic foci in and around the walls of the larger veins. (2) The complete replacement of the vascular layer by the specific infiltration. All of these changes, as a rule, are more advanced in the iris and ciliary body—another point in favour of the theory that the virus enters through the wound.

The infiltration is to be found in its purest and heaviest form in the circumpapillary and macular regions of the choroid. Here the least damage is done at the time of the perforation and here the layer is the thickest and the blood supply the richest.

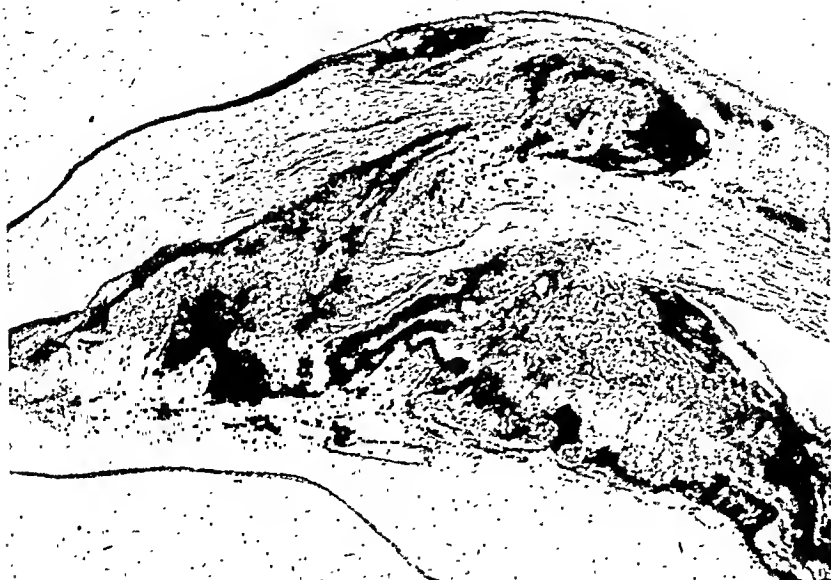


FIG. 1.

Tumour-like extra-ocular nodule of specific infiltration replacing prolapsed iris and simulating staphyloma.

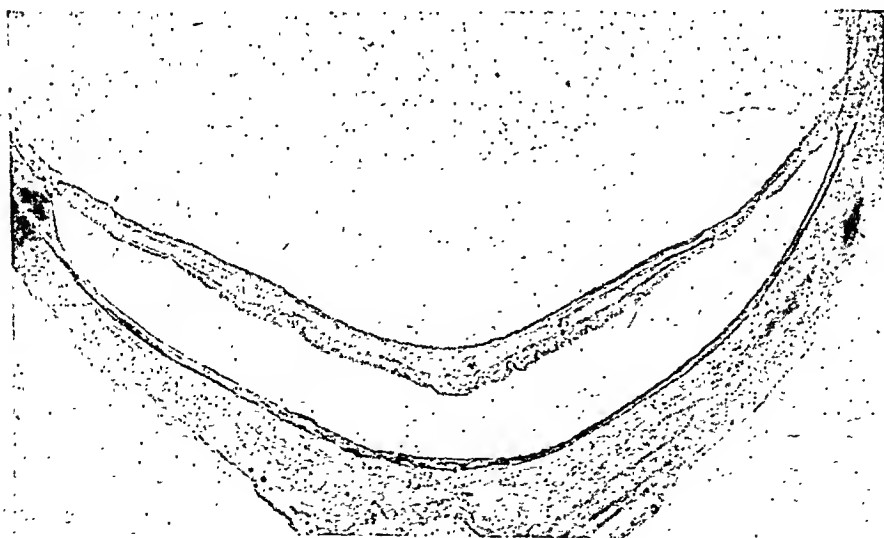


FIG. 2.

On either side a large dense nodule marks the point at which the retina becomes detached and the specific infiltration ends.

B. *Pathway of the virus through the globe into the tissues of the orbit.* The virus, judging always by the presence of the infiltration, leaves the inner eye by the same routes as those chosen by the cells of a malignant melanoma of the choroid. It may infiltrate layer after layer of the sclera and at the same time pass through the preformed emissaria. Anteriorly, the root of the iris is a favourite site for the accumulation of the specific cells, thereby clogging the angle and accounting for secondary glaucoma. The pectinate ligament may be destroyed and files of lymphocytes may replace the tissue between the internal and external sulci, leading to the sympathetic staphyloma seen in the worst cases. Rarely nodules occupy Schlemm's canal. Posteriorly, the segment of the sclera facing the muscle funnel is pierced by numerous large emissaria for the passage of the short ciliary arteries and nerves. This part of the sclera may be considered as the dangerous zone for the egress of the virus just as the ciliary region is the dangerous zone for its ingress. The heavy choroidal infiltration passes by continuity into the lamina fusca of the sclera and replaces it. In sympathetic ophthalmia, as in malignant melanoma, every emissarium is a *locus minoris resistentiae*. The infiltration passes without hindrance through these openings to the episclera and the space of Tenon. The destruction of the outer layers of the sclera proceeds with that of the inner layers. At the same time the middle layers may be permeated with nodules. At the height of the infection the implication of the sclera, through and through, is an outstanding feature of sympathetic ophthalmia. The infected sclera may be thought of as fairly reeking with the virus (Fig. 3).

By the union of the parts the virus passes into the insertion of the inferior oblique muscle. Sympathetic nodules have been reported replacing muscle bundles as far as 10 mm. from the sclera. Foci of lymphocytes are not uncommonly seen scattered in the fat that fills out the muscle funnel.

C. *Pathway of the virus into the optic nerve.* The infiltration in the choroid presses through the emissaria that surround the scleral canal into the sulcus of the intervaginal space of the optic nerve where a large number of cells may accumulate. On the way through the sclera the circle of Zinn may be enmeshed. Lymphocytic foci develop particularly along the pial sheath (Fig. 4). There is thus set up a sympathetic leptomeningitis of the intervaginal space. The infection is transmitted into the stem of the nerve by the pial sheath and the septal system derived from it; very rarely a typical nodule may be found some 12 mm. back of the lamina cribrosa. It is important to state here that the sheaths of the optic nerve are involved only in far advanced cases. The choroidal infiltration may make its way forward around the



FIG. 3.

The outer and inner layers of the sclera in the posterior quadrant are undergoing destruction. Lymphocytic foci are scattered in the middle layers. The overlying choroid shows an infiltration of lymphocytes, epithelioid cells and giant cells in its purest form. Similar elements have replaced the external layers of the sclera.



FIG. 4.

Files of lymphocytes infiltrate and separate the layers of the pial sheath. Note that infiltration extended beyond the point of excision.



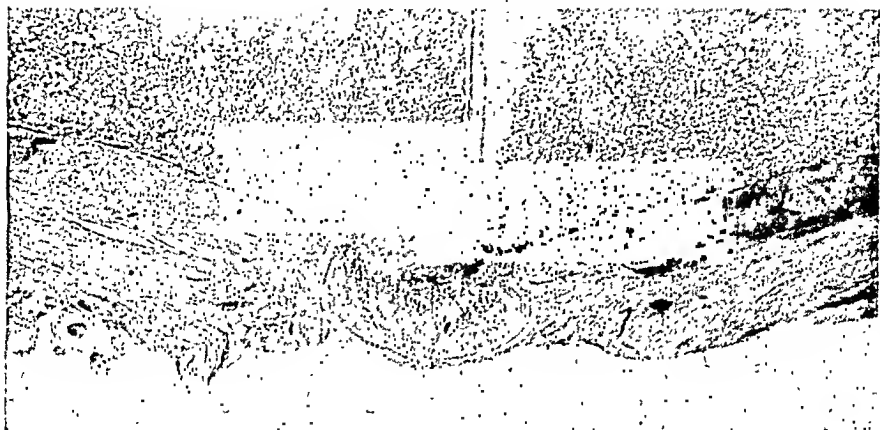


FIG. 5.

The optic nerve was excised within the scleral canal no doubt leaving much infected material behind. Small lymphocytic foci can be made out in the fat to the left.

opening in the lamina vitrea and appear as a collar surrounding the papilla. It is certain that the infection is not transferred to the other eye through the optic nerve and chiasm because the opposite nerve never shows signs of ascending inflammation.

#### ENUCLEATION OF THE EXCITING EYE

McKenzie, who in 1835 wrote the first scientific description of sympathetic ophthalmia, seems to have made no suggestion as to its prevention, although, he prescribed a number of palliative remedies. It remained for Prichard, in 1851, to advise the excision of the injured eye, but only after the fellow eye began to show signs of inflammation. In a few cases, probably those in the prodromal stage, the removal of the offending eye did arrest the process in the uninjured eye, thus adding further proof to the sympathetic nature of this disease. In most cases the condition continued to grow worse and in a few it seemed to be actually aggravated by the excision of the injured eye so that there grew to be considerable opposition to the operation.

Later, the crowning surgical step was made by Critchett, who advised the removal of the injured eye before there are any signs whatsoever of iridocyclitis in the other. In the active stage of any form of iritis Critchett took a strong stand against any attempt to perform an iridectomy, an operation which had been greatly overestimated as a cure for all kinds of iritis. It is the universal practice to-day to excise at once every globe which after a perforation shows

retraction of the wound, hypotony, sensitiveness either spontaneously or to light touch, and failing vision.

The object now is to apply with discretion the histological facts to the procedures for the removal of the exciting eye. Whenever enucleation is performed as a preventive measure the ordinary method of cutting the nerve on a level with the outer surface of the sclera may be employed with safety. Once signs of sympathetic ophthalmia appear the only hope of saving the uninjured eye lies in the immediate removal of the source from whence came the invasion and from which fresh virus would constantly be sent forth. Before operating it is possible to gain valuable information from examination of the sympathising eye as to the state of the infiltration in the injured eye and its appendages. If central synechia of the iris can be partially broken up and kept under control it is likely that the infiltration is in the first stage in the injured eye or at least is still intra-ocular. Should the iris be swollen and discoloured or, most important of all, should the pupillary zone be hopelessly bound down, these are signs that the inflammation has reached its acme in the exciting eye and that the extra-ocular structures are infected. The difficulty of removing an acutely irritated and painful globe surrounded by orbital cellulitis seems to account for the many instances in sympathetic ophthalmia in which the optic nerve is cut within the scleral canal. A long strip of the inferior oblique muscle should be excised and the optic nerve and the retrobulbar tissues around it should be removed almost to the apex of the muscle funnel. The wound should be left open to drain. If there remain in the exciting eye some degree of vision it is axiomatic to postpone enucleation as the benefit of the operation is always problematical and there is no justification for sacrificing even the faintest vision.

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## LINDAU'S DISEASE—PROGRESSION IN AFFECTED FAMILY

BY

ALEXANDER E. MACDONALD

TORONTO, CANADA

It is unfortunate that Lindau's disease has been inextricably associated with allied conditions in so many published reports of the clinical findings and pathological records. It is a rare condition, and to substantiate the diagnosis it seems reasonable to require that the presence of multiple haemangioendothelioma be verified, for at

least one member, with a similar tumour in another member of the family. It seems certain that this will happen more frequently during the life of the patient, as the advances made in surgery of the brain indicate that earlier diagnosis is probable.

We have had the opportunity to follow the course of Lindau's disease in a family where three of the four members of a sibship has each undergone the successful removal of cerebellar tumours, which on pathological examination proved to be haemangioendothelioma.

The death of sibling two, a female, occurred  $3\frac{1}{2}$  years after the cerebellar tumour was removed from sibling four, the youngest and only male in the family. All four members have had eye involvement, and sibling two had a cataract, in a glaucomatous eye which after extraction of the cataract developed pain so severe that enucleation resulted. The early pathological report showed that a retinal detachment due to intra-ocular haemorrhage was present, and it was only after sibling one had a cerebellar tumour removed and verified as a haemangioendothelioma that a further search was made for the presence of a tumour in the enucleated eye of sibling two. A haemangioendothelioma was found when further sections were made and the findings reported in the Transactions of the American Ophthalmological Society, Vol. 37, 236-250, 1939, and Archives of Ophthalmology 23: 564-576, 1940. The interest in this remarkable family, which produced for several years three verified living cases of Lindau's disease, may justify the following brief review of the present status of the various members and the clinical report of sibling IV who previously was reported as being healthy.

#### REVIEW

In 1912 the mother of this family, at the age of 22 years, had a painful eye enucleated, according to Dr. Wilber Fraser of Ottawa who found the record in Dr. Minnes' files. The globe was opened and a complete cup-like calcification of the choroid was found, but no microscopic sections were made. The family state that her death resulted after an operation for a brain tumour in 1918, but no record of this could be found at the hospital in Ottawa.

*Sibling II*: In 1934, while bending over, suddenly lost the sight of her left eye, due to an intra-ocular haemorrhage. On February 24, 1936, at the age of 23 years, at a second stage cerebellar exposure a vascular tumour the size of a walnut, which pressed on the medulla, was found in the lower hemisphere. The upper part of the spinal cord was cystic.

Roentgen therapy was administered to the region, seventeen



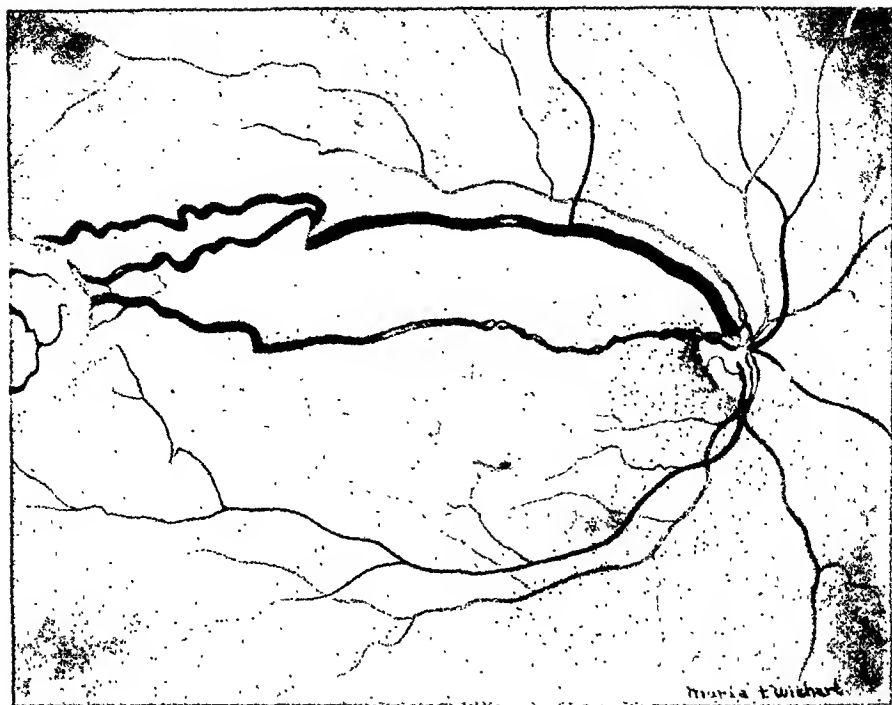


PLATE I.

Fundus O.D. of Sibling I before radon treatment ; showing detachment about peripheral tumour and dilated vessels.

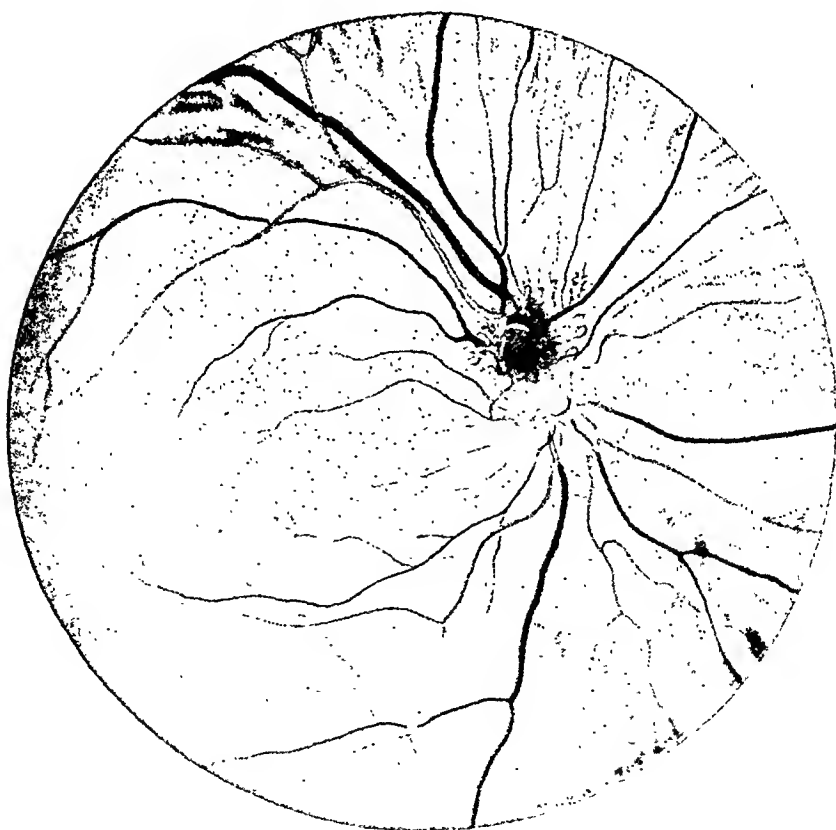


PLATE II.

Fundus O.D. of Sibling IV before radiation. The capillary angioma covers the upper part of the disc and extends into the retina above.

times, and she was re-admitted for vomiting caused by this treatment.

March 30, 1937: Left cataract extraction.

May 31, 1937: Enucleation L.E. blind and painful due to secondary glaucoma. The pathological report of this eye at first showed that the detachment of the retina was due to intra-ocular haemorrhage. A re-examination was made in April, 1939, and a haemangioendothelioma was found and reported.

August 10, 1939: A cystic cerebellar haemangioendothelioma was removed and verified by pathological examination. Following this she remained well and carried on her work as a nurse until headaches and unsteadiness of gait developed early in 1947.

August 5, 1947: At a re-exploration of the cerebellum two large tumours were found; one was the size of a hen's egg, the smaller in the roof of the fourth ventricle. Both were removed, and it was found that the tumour infiltrated the muscles of the neck.

August 8, 1947: Following the operation she developed signs of medullary failure, was unable to swallow, and died. The autopsy revealed multiple cysts of the pancreas, kidneys, chronic interstitial pancreatitis and terminal broncho-pneumonia.

*Sibling I*: Female, aged 29 years.

May 6, 1938: A haemangioendothelioma, verified by pathological examination, was removed from the left cerebellum. This firm tumour was the size of a walnut. It was attached to the dura, lateral sinus and tentorium by large thin-walled vessels, which contained arterio-venous blood. For three years she had noticed a loss of vision in the right eye. The fundus showed central degenerative changes and her visual field showed a lower nasal defect which extended to 40 degrees from central fixation. With a widely dilated pupil, a whitish mass with a haemorrhage on its surface was seen well out to the periphery. The upper temporal vessels were greatly dilated (see plate I).

May 28, 1939: Four radon seeds of 0.7 millicuries each were placed subconjunctivally on the sclera, opposite the site of the tumour and removed seven days later. The seeds were tied separately to a silk thread and this part of the suture was dipped in thin pyroxylin solution. Moderate reaction followed at first, but for many months a depression at the treated area remained on the globe. Possibly one-half the dosage would have been sufficient to destroy the retinal tumour.

March 30, 1942: She complained of staggering, weakness of left arm and difficulty in controlling her speech. At this time  $RV=C.f.$  at 2 m and  $LV=6/18$ . The right eye was divergent 40 degrees.

April 24, 1947: A tumour the size of a walnut was removed from approximately the same area as at the previous operation. Dr. Eric

Linell reported the tissue as being extremely cellular. The cells were uniform in size with fusiform nuclei and a moderate amount of cytoplasm. The cell boundaries were indistinct. Some large blood channels were present but the Mallory stain showed capillary-like channels in large numbers. No mitotic figures could be seen with the cresyl violet stain.

August 6, 1947: The family stated that she still complained of unsteadiness of gait and deafness in the left ear, but she was able to do her housework.

*Sibling III*: A female, was re-examined on August 6, 1947. The naevus on the limbus of the left eye was less distinct than when seen in 1938. She looked well and stated that her health had been good.

*Sibling IV*: A synopsis of his voluminous history follows: Flt. Sgt. W. R., a white male, aged 27 years, began to complain of headaches, which were worse when he was in the prone position and during the morning. They were severe and gradually became worse. In July, 1942, he overturned a plane while landing it, and a careful physical examination followed. His history was referred for advice to Dr. K. G. McKenzie, who recalled the family history and asked for his admission to Christie Street Military Hospital, as from the record the presence of a brain tumour was considered possible.

January 28, 1943: The vision in each eye was normal with correction. The fields of vision showed only a slight enlargement of the blind spot in the right eye and the fundi were reported as being normal, but one week later it was stated that the right disc showed blurring on the upper and nasal borders with a moderate physiological cup. The left disc showed a slight haze at the upper border. Horizontal nystagmus was present, bilateral, more marked on looking at the right. The gag reflex was absent, the electrocardiograph negative. The impression was that the relative hypertension 154/114, nystagmus and absent gag reflex might be due to hyperinsulinism, an adrenal or intracerebral tumour.

February 2, 1943: Dr. McKenzie, in view of the above examination, combined with the family history, injected the ventricles and found the left lateral hemisphere under pressure, the whole ventricular system was enlarged and the picture suggested the presence of cerebellar angioma. He was transferred to the Toronto General Hospital for the operation.

February 27, 1943: A vascular tumour the size of a walnut was found in the angle between the right tonsil and the cerebellar hemisphere which shelled out by finger dissection. See Figs. 1 and 2. The post-operative treatment required a re-opening of the wound to remove an extra-dural blood-clot that developed within



FIG. 1.—SIBLING IV.

Medium power  $\times 120$ . Mallory connective tissue stain showing many vessels with fibrous walls, the intervening spaces being filled with endothelial cells.



FIG. 2.—SIBLING IV.

Bisected tumour,  $35 \times 30 \times 15$  mm. showing fibrous structure and cystic degeneration.

24 hours, but by March 5, 1943, he was well enough to be transferred to his military hospital. At this time he had a marked horizontal nystagmus, dizziness and bilateral 6th nerve paralysis with right sided inco-ordination, but five days later he was able to sit up. One week later he could walk with help.

April 7, 1943: No headache and no diplopia was present, but there was slight inco-ordination of both hands and feet. He was discharged to return for a check-up visit in six months.

April 9, 1947: He was re-admitted to Christie Street Hospital



complaining of fatiguability, dysfunction of balance and slight loss of hearing of the right ear.

Laboratory examination.—Sedimentation rate 16 mm., urine acid, specific gravity 1021, negative for albumin and sugar, Kahn negative. Examination revealed no corneal reflex and cranial nerves essentially negative. Personal history: He had returned to work two months after his operation, as a checker in a lumber camp, but at the time of this admission he had been teaching in a school.

February 2, 1947: The fields of vision showed slight enlargement of the right blind spot. The pupils were equal in size, reacted to light and convergence, full ocular movements were present with no nystagmus. The disc of the right eye showed a reddish elevation over the upper half with new blood vessels. The superior temporal vein was engorged. Radiation was suggested for this developing angioma. He was seen also at this time by Dr. McKenzie, who found no evidence of a recurrence of the brain tumour.

June 10, 1947: See colour drawings of the right fundus showing angioma.

August 15, 1947: R.V. 6/12-1. L.V. 6/9-2.

In the fundus of the right eye the media were clear. There was considerable connective tissue over the upper part of the disc with new loops of capillaries extending up into the retina. These were elevated about three dioptres. The mass was purplish-red and extended down over the cup. The fundus of the left eye essentially negative, only a slight crescent and clear, physiological cup. Partly on account of his obligation to teach in September and his good vision, he requested that the treatment be delayed. He stated that his four children: girl of 8, boy of 6, girl of 2 and a one-month old boy were well.

January 10, 1948: Fourteen treatments have been given to the area of the developing eye tumour. The vision R.V.=6/18, L.V.=6/12 and normal in each eye with correction.

The right fundus showed an area of grey oedema over the tumour mass which was seen with a plus four lens. Above the disc the capillary loops extended higher into the retina when compared with the drawings made in May, 1947.

#### DISCUSSION

The familial condition where multiple capillary haemangioendothelioma occur in the cerebellum, cerebrum, retina, spinal cord, kidneys, pancreas, epididymis, liver and bone, with occasionally hypernephroma, should be termed Lindau's disease.

A review of a family and the most recent case history in the only male has shown that the cerebellar tumour was verified for sibling I at the age of 29 years by pathological section and an eye tumour was treated by radon seeds. Sibling II—the cerebellar tumour was verified at operation at the age of 23 years and by pathological section at two subsequent operations. The eye tumour presented a similar pathological appearance. Sibling III had a naevus of the limbus of the left eye, which became less apparent after nine years. Sibling IV: The new case was verified by pathological examination at the age of 28 years and after extensive radiation an eye tumour, capillary in type, has slightly progressed in four years.

*Acknowledgment:* To Dr. K. G. McKenzie my thanks and congratulations for the surgical care and remarkable results that have meant so much to the members of this family. Dr. Eric Linell was responsible for the excellent pathological reports and photographs. Miss Wishart made coloured drawings, which add much to the written description. Also thanks to the Departments of Surgery, Neuro-Pathology, Veterans' Affairs, Ophthalmology, Art and Photography.

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## METHODS OF INVESTIGATING EYE MOVEMENTS

BY

H. HARTRIDGE *and* L. C. THOMSON

VISION RESEARCH UNIT, MEDICAL RESEARCH COUNCIL,  
INSTITUTE OF OPHTHALMOLOGY, LONDON

OPINIONS differ widely at the present time with regard to the ability of a subject to perform accurate fixation, for whereas some hold that the eye is constantly making rapid oscillations, on the presence of which visual acuity for fine detail actually depends, others hold, on the contrary, that such oscillations are absent in normal subjects and that if these movements were present, far from aiding the perception of detail, they would have the effect of seriously interfering with it. Thus Hering (1899) thought that the irregularities at the contours between the images of objects which are produced by the retinal mosaic are smoothed by chance eye movements. Anderson & Weymouth (1923), Averill & Weymouth (1925), and Marshall & Talbot (1942) have held similar views, and they have extended the consideration to the cases of small differences of size and small defects in alignment. Wright (1942) claims that the eyes are continually performing "twittering" movements, and that in consequence the receptors are able to scan the retinal image in the same way that the bright spot in the cathode ray tube of a television receiver scans the fluorescent screen. He writes, "It is the dimensions of the cones rather than their number

which is the essential factor in determining the visual acuity." Thus a sparse population will perform as well as or even better than a dense one. Adler & Fliegelman (1934), as the result of recording the reflection of a beam of light from a galvanometer mirror which had been attached by surface tension to the sclera of a subject, claimed to have demonstrated the presence of fine oscillatory rotations of the eyeball. Lastly Lord & Wright (1948) have stated that they find evidence which confirms that of Adler and Fliegelman, because their records show that the subject's eye is oscillating with an amplitude of about thirty minutes of arc.

In contradistinction to these views experiments were performed by Hartridge (1947) which were based on the employment of very precise fixation. Thus the position of the fixation points for rays of different colour at the fovea appeared to be identifiable within a fraction of a cone unit, and as a rule ophthalmologists do not find that eye movements interfere with observations of the anterior eye structures by means of the slit-lamp, in which magnifications of between fifteen and thirty diameters are normally employed.

## SECTION 2: PROBLEMS CONNECTED WITH THE OBSERVATION OF EYE MOVEMENTS

A number of different methods have been employed in the past for investigating the movements of the eye. It is not proposed to consider these in detail in this paper, but instead to concentrate attention on optical methods alone, since in the opinion of the authors these are more likely to lead to accurate results than are methods which depend on other principles.

Three main problems have to be faced in designing a satisfactory technique.

- (a) Obtaining the necessary accuracy.
- (b) The elimination of chance movements of the head.
- (c) Eliminating the effects of the heart beat.

With regard to the first problem the precision needed corresponds to a rotation of the eyeball of one minute of arc. This is the minimum precision which should be aimed at. If a method could be devised which provided a precision of one-tenth of this, that is six seconds of arc, it would be advantageous because one cone unit, namely 2 mm. at 10 metres, the standard proposed by one of us elsewhere (1947), corresponds to an angle of 41.236 minutes of arc, and it would be an advantage therefore to be able to express the rotation of the eye in terms of cone units and fractions of a cone unit. If a human eye rotated through an angle of one minute of arc the various parts forming the coats of the

eye would suffer a rotatory displacement of about  $2.4\mu$ . The optical method therefore has to satisfy the requirement of being able to provide measurement of such a displacement to at least an accuracy of  $2.4\mu$ , and if possible to an accuracy of  $0.24\mu$ .

With regard to chance head movements these are frequently quite large. The precise cause of them is not known. It may be that they are due merely to irregularity in the contraction of the muscles which support the head on the body, and to similar irregularity in the muscles which maintain the position of the body. Another possibility is that the proprioceptive control of the head in relation to the environment lacks high precision. Whatever the cause may be there is little doubt that the head is constantly performing small nodding movements, both lateral and anteroposterior. These are largely counterbalanced by compensatory rotations of the eyeball which, in spite of head rotations, maintain the gaze on external objects. The study of eye rotations during the rotation of a subject, by means of a cinema camera mounted on the same turntable as himself, had already provided us with much information with regard to these compensatory rotations of the eye, but there is little doubt that much remains to be learnt concerning them.

With regard to the effects of the heart beat the eye itself appears to be so arranged in the orbit as to be immune, or almost immune, from the effects produced by variations in blood flow during the various phases of the cardiac cycle. The effects of the heart beat most strongly assert themselves either when apparatus is mounted on the head, attached to a plaster hat, or when attempts are made to immobilise the head by means of pads or clamps externally applied. Because of these circulatory effects in the soft tissues of the head it would appear to be a matter of considerable difficulty to immobilise the head completely. It will be recollected that even the teeth are not in solid contact with the bones of the upper and lower jaws, but that they are inserted into soft tissues which are themselves supplied with blood and therefore pulsating to some extent with the heart beat.

### SECTION 3: THE CHOICE OF SUITABLE EYE STRUCTURE

It is obvious that theoretically any structure accessible to light may be utilised for recording optically the rotations of the eyeball. It is therefore largely the practical considerations which decide what structure provides advantages over others. It is not possible to contrast all the possible structures which are available. A few of the more important only will be considered in this paper.

*The cornea.*—This structure has two advantages. It is readily

accessible and its anterior surface reflects light in the same way that a convex mirror of short radius of curvature reflects light. It was for these reasons that at the suggestion of one of us Vernon made use of the reflection from the cornea, when studying the eye movements which occur during reading.

The corneal reflection has one disadvantage, namely that the movement of the reflected image of the light source is not as great as the actual movement of the anterior surface of the cornea itself but is about half the movement. In order therefore to measure the rotations of the eye with a precision of one minute of arc it would be necessary to be able to measure the movement of the corneal reflection with a precision of about  $1.8\mu$ . There is another disadvantage in using the corneal reflection, namely that deflections may take place owing to alterations in the local thickness of the lachrymal fluid. This is very likely to occur if the reflected image is taken off the eyeball near the margin of either the upper or the lower lid, or if any factor connected with the observations is causing lacrymation.

*The iris.*—This structure in subjects whose irises are not deeply pigmented provides an admirable object for photography, the obvious disadvantage attending its use being the constant alterations in the diameter of the pupil which are all the time taking place in normal subjects. These difficulties may in large measure be avoided by paralysing the iris, either in its dilated condition by means of atropine or in its contracted condition by means of eserine. The line of demarcation between the edge of the iris and the pupillary aperture under either of these treatments provides a sharp edge by means of which the necessary precision should be obtainable. There is one disadvantage however, that it is not easy to illuminate the substance of the iris brightly without at the same time flooding the eye with light. To some extent this difficulty can be offset by directing the illuminating beam towards the subject's blind spot.

*The sclera.*—The sclera may be utilised under three conditions.

(a) Where the scleral vessels are partially engorged with blood so that they provide the necessary landmarks for photography.

(b) Where a suitable part of the sclera has been tattooed.

(c) Where a suitable foreign body has been placed in contact with the sclera.

Adler and Fliegelman applied a plane mirror to the sclera allowing it to adhere by surface tension. The disadvantage of this technique was that rocking of the mirror could take place owing to the fact that the sclera was curved but the mirror flat. One method of overcoming this difficulty would be to employ a concave lens, the concavity having the same radius of curvature as the

of the sclera, the other side of the lens being polished flat or to a suitable curvature and made reflecting by means of aluminium, silver or rhodium. Such a lens-mirror should not be found to rock during the rotations of the eye. Another method has recently been used by Barlow, namely to apply small drops of mercury to the sclera, and to use these as landmarks. The only difficulty which is likely to be met with here is that the mercury droplets may be slowly swept along in the lacrymal fluid which is emerging under the border of the upper lid and is flowing towards the inner canthus of the eye.

*The retina.*—The retina would appear to have obvious advantages over all the structures which have been previously mentioned, owing to two factors; (a) it is the structure which is vitally concerned with movement because it is the movement of the image of the lens system relative to the retina with which we are concerned when studying eye movements, and (b) due to the fact that the retina rotates in one direction, when the lens system is rotated in the opposite direction, the apparent movement is double that obtained when making observations on the superficial eye structures which have been mentioned above. The difficulties likely to be met with in practice are those connected with the illumination of the retina, and in the provision of a sufficiently fast film for adequately recording the somewhat feeble light which re-emerges through the pupillary aperture. By choosing a subject with slight retinal pigmentation and by directing the illuminating beam at the blind spot, which is as a rule paler than the rest of the retina, it should be possible to obtain sufficient illumination without at all seriously disturbing the retina and preventing adequate fixation.

*The contact glass.*—It is obvious that if a contact glass could be fitted to the subject's eye, so well-fitting that it moved precisely with even the smallest rotations of the eye, and not at the same time causing painful sensations, it would go a long way to providing the solution of many of the problems indicated in earlier parts of this section, thus the artificial cornea could be given a curve of a much smaller radius than the real cornea, the consequence of which would be that the ray reflected from its surface would undergo a bigger movement for a bigger rotation of the eye than the subject's real cornea. A long-sighted subject is preferable for such a method; because in order to correct his long sight a contact lens with a more highly curved cornea would be indicated. Secondly it would be possible to mount a galvanometer mirror on such a contact lens just to one side of the cornea. There would be no possibility of such a mirror rocking during eye rotations, as might be the case if the mirror were attached directly to the sclera. Thirdly it would be possible to engrave suitable

marks either on the centre of the artificial cornea or to one side of it, or on the artificial sclera, at will, but as indicated above the method would only succeed if the contact lens precisely fitted the curvatures of the subject's eyeball, so that there would be complete absence of "backlash" between the eyeball and the contact lens.

Reference has already been made to the fact that whereas the corneal reflection moves less than the cornea itself, for a given rotation of the eye, the apparent rotation of the retina is double that of the cornea, because it is being viewed via the lens system of the eye. It may be useful to summarise the efficiencies of the other structures mentioned above.

TABLE

<i>Structure</i>	<i>Efficiency</i>
Corneal reflection	0.5 - 0.4
Iris	1.0
Sclera	1.0
Retina	1.9 - 2
Scleral mirror	3 - 4

It will be seen that according to the above table the scleral mirror provides the most efficient optical arrangement.

#### SECTION 4: SOME SUITABLE OPTICAL ARRANGEMENTS

There are broadly two optical methods which may be adopted for determining the eye movements. One consists of photographing the movements after suitable magnification, by means of a cinema or other camera. The other consists in utilising two or more photoelectric cells and amplifying and recording the currents which are generated in these. The relevant pros and cons of these methods are difficult to assess but both should give satisfactory results. The first method has been used recently by Hartridge and Thomson, the latter method is in use by Lord and Wright. When their method is used the subject lies on his back, his head resting in a ring; suitable supports are placed on either side of the head; a mouth plate is also employed. In these various ways head movements are restricted. Actual head movements are recorded by means of an artificial cornea which is attached to a suitable fitting which clamps on one of the front teeth. Both head and eye movements together are recorded by causing rays of light from an ultra-violet lamp after reflection in the corneal surface to fall on two photo cells, in front of which are placed knife edges in order to cut off part of the reflected beam. When

the cornea moves the beams of light are deflected. In consequence more or less light falls on the photo cells. The voltages on the cells after suitable amplification cause excursions of the fluorescent point of light in cathode ray tubes, and these are recorded photographically in the ordinary way. Continuous records are obtainable. So far they have not devised apparatus which will record both head and head and eye movements at the same time, so that they have not obtained eye movements independently of head ones.

The present method used by Hartridge and Thomson consists of a low-powered microscope, which is attached to a plaster of Paris hat which fits on the subject's head. This hat also carries

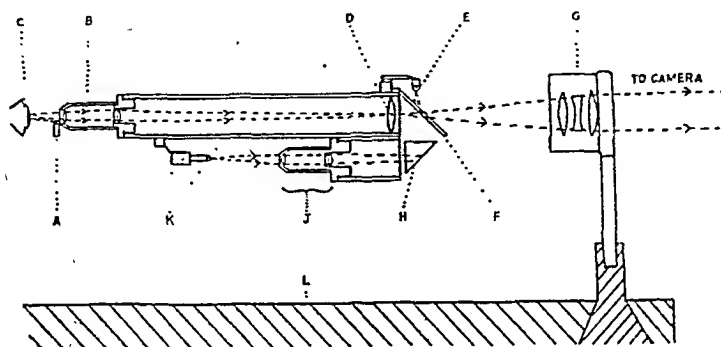


FIG. 1.

A plan of the original apparatus used by Hartridge and Thomson to measure movements of the eye.

A, light source to provide the corneal reflection; B, microscope objective; C, cornea; D, field lens; E, reference source; F, sloping glass plate to introduce reference image; G, collimator; H, right-angled prism; J, objective for the introduction of the fixation spots; K, source of light for fixation; L, optical bench.

the light source for illuminating the cornea, a reference source which is photographed alongside the magnifying reflection of the corneal image and a fixation light source, which by suitable optical means provides the subject with two bright points of light, on either of which at will he may preserve fixation. The low-powered microscope has such a focal length that the source of light, after reflection in the cornea and re-magnification, has approximately the same dimensions as the reference source. The latter is introduced into the light beam by two reflections at an unsilvered glass plate. In consequence two images of the reference source are seen by the camera. This duplication is found to assist the subsequent alignment and measurement of the photographic film. The cine camera which takes up to sixty frames per second is focused at



infinity, and the rays from the low-powered microscope attached to the subject's head, after passing through a field lens, enter a collimator lens which is attached to an optical bench. The optical bench to which the camera is attached is fixed to an independent

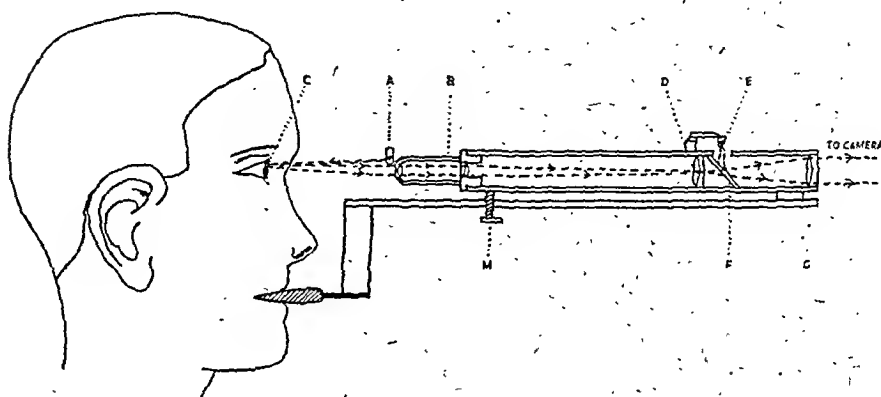


FIG. 2.

A plan of the new apparatus for measuring eye movements. Lettering as for Fig. 1, except that M indicates a screw for vertical height adjustment.

table, so that vibrations set up by the motor of the camera are not conveyed to the apparatus attached to the hat of the observer.

A new type of apparatus has recently been devised by Hartridge and Thomson, namely to hang from a suitable counterpoise a frame which carries the microscope, the reference lights and the

:        :        :        :        :

FIG. 3.

Five frames from a cine film taken at a speed of 64 frames a second, showing an intentional eye movement. The central frame shows the two reference images lying beside the moving corneal reflection.

corneal light source. It also carries a mouth plate which fits on to the teeth of the subject. The counterpoise is so arranged that the apparatus tends neither to rise nor to fall, but can be freely rotated in all directions. The optical apparatus is so disposed that the subject can observe uninterruptedly suitable fixation points of light which are attached to a wall beyond the apparatus. This

apparatus retains the advantage of the previous one, of enabling measurements of eye movements to be obtained which are quite independent of head movements. It has three other advantages. In the first place no constraint need be placed on head movements



FIG. 4.

An enlarged image of a single cine frame from a strip of film taken during fixation of the eye. The corneal is the unpaired image on the right.



FIG. 5.

An enlarged image of a single cine frame from a strip of film taken during an intentional movement of the eye.

and no difficulties arise through attempting to immobilise the subject's head. In the second place the head movements relative to the camera may be determined by the movements performed by the images of the reference lights. Lastly since the optical equipment is not fastened to a plaster hat which rests on the subject's

head, fluctuations in vascularity do not affect the position of the apparatus in relationship to the eye.

A diagram of the old apparatus employed by Hartridge and Thomson and a diagram of the new apparatus now under construction are shown in Figs. 1 and 2. In Fig. 3 is shown an enlargement of a short length of cine film showing an intentional vertical eye movement. In Fig. 4 is shown an enlarged image of a single corneal reflection. Such fine definition would be impossible if the eye were performing very rapid vibratory rotations. Fig. 5 shows an enlarged image of a corneal reflection photographed whilst the eye was performing an intentional eye movement.

One millimetre on Figs. 4 and 5 corresponds to a displacement of the image on the retina equal to  $28\ \mu$ , that is, to 83 cone units.

### SECTION 5: THE EXAMINATION OF THE PHOTOGRAPHS

Three methods have so far been used for examining the cine film: (a) The detailed examination of single frames with a low-power microscope; (b) the projection of lengths of film on to a screen at one-quarter the speed at which they were taken; (c) the measurement of selected frames, using a microscope which has been fitted with a Leitz mechanical eyepiece micrometer. The latter method was found to be very laborious.

A fourth method, which is to be tested as soon as the necessary apparatus is available, consists in the preparation of an enlarged negative of one frame of the film and then the projection of the magnified images of other frames on to this enlargement, the magnification used being the same as that employed during the making of the enlargement. This method requires a special microscope having two mechanical stages, one about 200-250 cm. above the other, between the two being mounted a projection lens of short focal length. On the lower stage is placed the film strip and on the upper one the enlarged negative. The projection lens, which magnifies about 8 times, now produces an image of the film in the plane of the enlarged negative.

Using the horizontal and vertical adjustments the corresponding parts of the images of the filaments of the reference lights are now superposed, and adjustments are made until an exact fit is obtained. Now if the frame and the enlargement are alike, the consequence will be that when the images of the reference light are in exact superposition the images of the corneal reflection will be in exact superposition also. If on the contrary they are unlike, owing to a rotation of the eye, then a movement either of the film strip or of the enlargement will be required in order to superpose first the images of the reference light and then that of the corneal light, and this movement will be a measure of the eye movement which

has taken place between the exposure of the frame from which the enlargement has been made and that now being examined. It is hoped that this method will enable the films to be examined with the required accuracy at a rate of about one frame every two or three minutes.

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## TISSUE CULTURES OF MOUSE LENS EPITHELIUM

BY

IDA MANN

*From the Laboratories of the Imperial  
Cancer Research Fund, London*

It has been pointed out by Kirby<sup>1</sup> that if an attempt is made to grow the lens in tissue culture the only cells which survive and multiply are those of the subcapsular epithelium. This is to be expected since the lens fibres are fully differentiated and cannot divide. Kirby's preparations were made with the lenses of chicks. In the present experiments an attempt was made to grow mammalian lens epithelium in tissue culture.

#### EXPERIMENTS

Mice were used, mostly of the inbred strain known as C3H. Lenses of young mice up to 10 days old were used first but proved difficult to plant out without infection. Lenses from embryo mice of the same strain were then tried, with greater success. The embryos used were in the later stages of the pregnancy and good results were obtained with full term embryos taken just before birth. With care uninfected cultures could be obtained in about 60 per cent. of the trials. About 70 cultures were made in all.

The culture medium which gave the best results had the following formula:—

Rat serum	...	...	1½ parts
Tyrode solution	...	...	1 part
Mouse embryo extract	...	1	part
Dist. water	—1-2 drops per c.c.		

## RESULTS

1. If the lenses were cultured free from all surrounding tissue and with intact capsules they survived for about 10 days unchanged, and no outgrowths occurred.

2. If the capsule was ruptured at the moment of planting it shrank and lens fibres and subcapsular epithelial cells were extruded. The lens fibres dissolved in the medium within the first 2-3 days. The capsule remained unchanged but the epithelium proliferated and grew away from it all round in a flat sheet of large globular clear cells. Fragments of the sheet tended to break away and float off, so that permanent preparations were hard to make. Most of the cultures were therefore photographed *in vivo*.

Differentiation could be seen in the cells of the culture around the tenth day, beyond which very few survived. The first stage of differentiation was shown by increase in the cytoplasm and movement of the nucleus to one side. In a few cells a further stage was reached, the voluminous clear cytoplasm apparently flattened so that the cell became bluntly pointed at both ends, the nucleus remaining applied to one side of the central part of the elongated portion of the cell. This movement of the nucleus to one side of the cell is the first stage in the process of normal differentiation of a lens epithelial cell into a lens fibre in the intact lens. It can be seen towards the equatorial region in horizontal sections of mouse and other mammalian lenses. The nucleus moves to the side of the cell next to the capsule, and the cell then elongates forming a lens fibre with the nucleus eventually equidistant from the two ends.

The accompanying figures are representative of the results obtained. Fig. 1 shows a stained preparation of a surviving intact mouse embryo lens at 6 days. The subcapsular epithelial cells stain deeply.

Fig. 2 shows a similar lens after 10 days survival. The staining is no longer uniform as most of the cells have disappeared over the anterior pole and the nuclei are pyknotic elsewhere.

Fig. 3 shows a mouse embryo lens growing in tissue culture at 3 days. The capsule was ruptured at the time of planting. Débris of lens fibres and beginning sheets of subcapsular epithelial cells surround the shrunken and wrinkled capsule.

Fig. 4 shows a culture at 6 days. The sheet of outgrowing epithelium is wider.

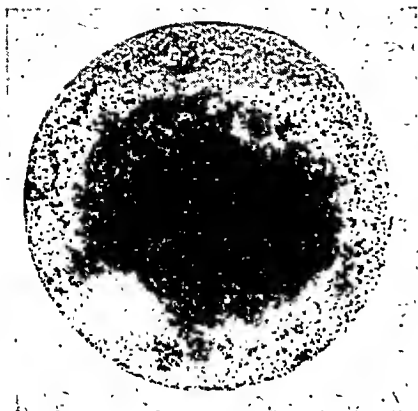


FIG. 1.

Intact surviving mouse embryo lens at six days, fixed and stained.

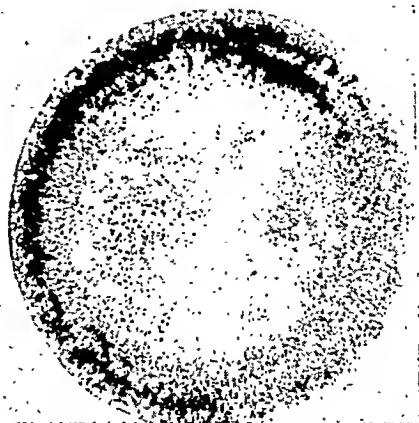


FIG. 2.

Intact mouse embryo lens in culture at 10 days. Fixed and stained. Many of the nuclei do not stain, many are pyknotic.

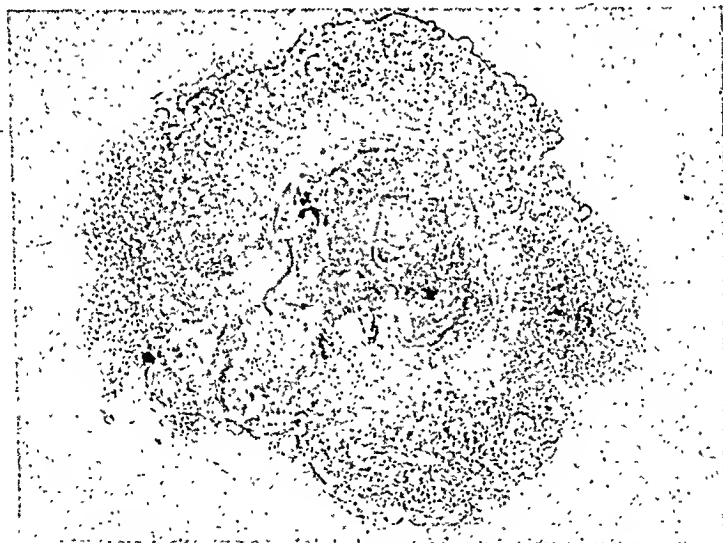


FIG. 3.

Mouse embryo lens with ruptured capsule in tissue culture at 3 days. Living preparation.



FIG. 4.

Mouse embryo lens with ruptured capsule in tissue culture at 6 days.  
Living preparation.

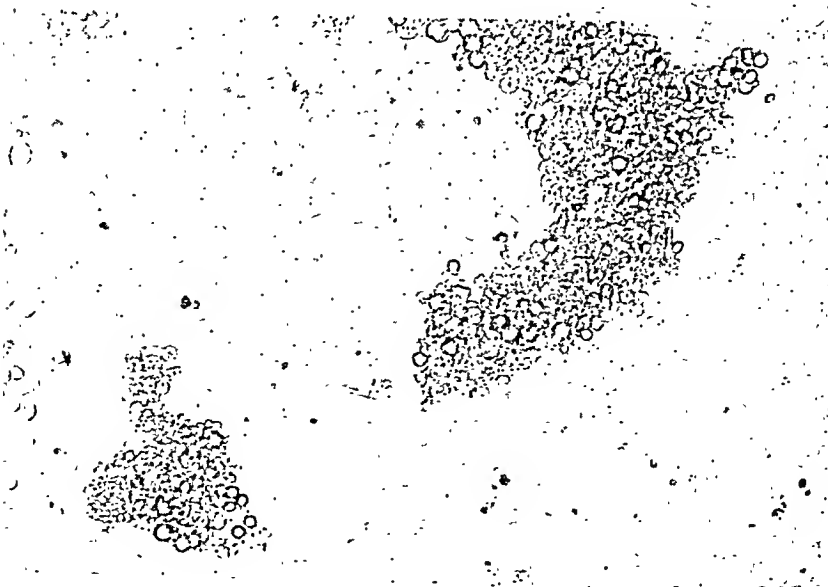


FIG. 5.

Portion of detached epithelial sheet from lens seen in Fig. 4. Living preparation.

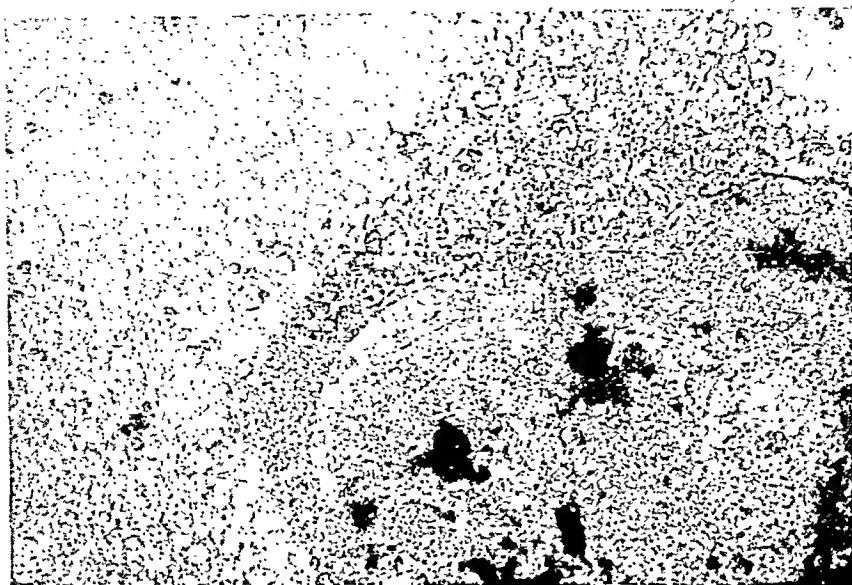


FIG. 6.

Full term mouse embryo lens growing at 11 days. Living preparation.

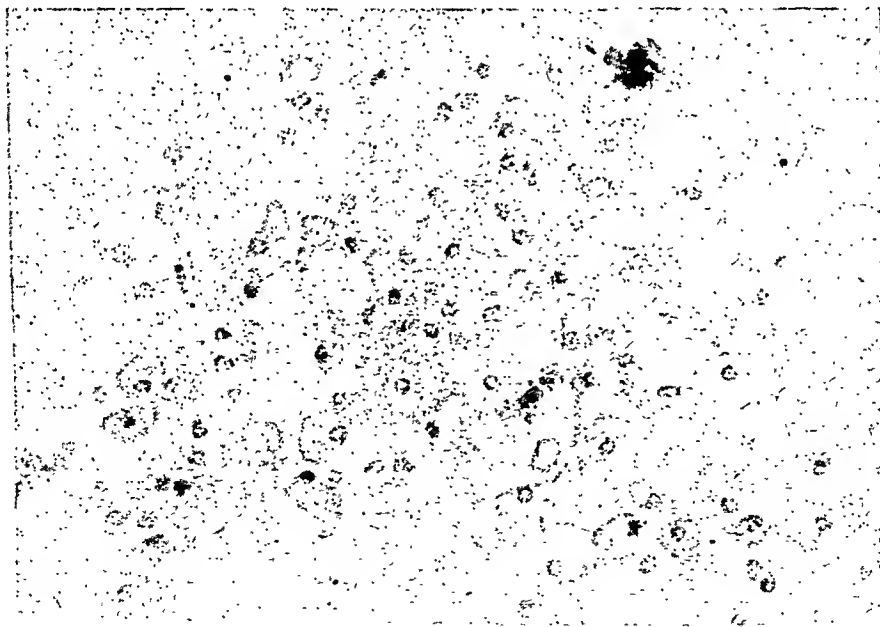


FIG. 7.

Epithelial sheet from mouse embryo lens tissue culture at 10 days.  
Fixed and stained with haematoxylin and eosin.



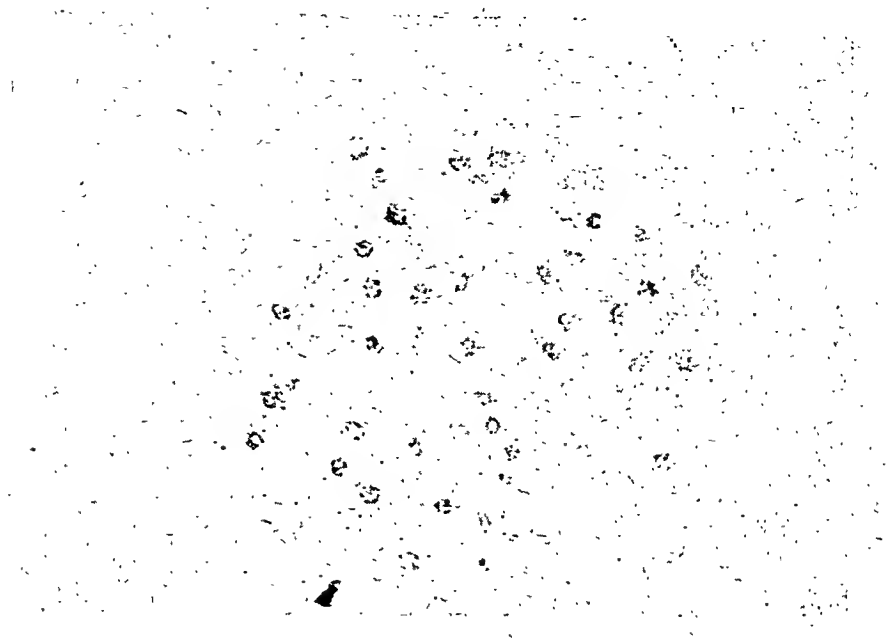


FIG. 8.

Similar to Fig. 7, but showing slightly more cellular differentiation.

Fig. 5 shows a portion of the epithelial sheet which has broken off from the explant and is floating free in the medium.

Fig. 6 shows a higher power view of the epithelial cells growing out from the capsule at 11 days. The embryo in this case was full term.

Fig. 7 shows an outlying portion of the epithelial sheet fixed and stained at 10 days. The position of the nuclei at the side of the cell and the large amount of clear cytoplasm is well seen.

Fig. 8 shows another portion of a similar sheet in which two at least of the cells show an attempt at elongation at both ends away from the nucleus. No culture remained alive after 12 days and no further stage of differentiation was observed.

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## COLOUR VISION, 1868 and 1948

BY

W. D. WRIGHT

IMPERIAL COLLEGE OF SCIENCE

"THE vast literature on colour vision consists almost entirely of papers written in support of some particular theory. It is peculiarly difficult to obtain a general and unbiased view of the subject, which demands a not inconsiderable knowledge of such diverse subjects as physics, physiology and psychology. I have here endeavoured to separate the best established facts of colour vision from the theories, and have then discussed the chief theories in the light of these facts."

In these words Sir John Parsons opened the Preface to his book "An Introduction to the Study of Colour Vision," and no more fitting comment could be made on the troubles that beset a student of colour vision. In a tribute such as this, it would be out of place to flog the merits of this or that theory, but it is intriguing to look back and compare the facts and theories of 1868 with those of the present day.

The year 1868 does not itself appear to be notable for any major scientific contribution to colour vision, but the period seems largely to have been dominated by the outlook of Helmholtz and Clerk-Maxwell. That, of course, is equivalent to saying that the Young-Helmholtz theory was widely accepted, as a result of the colour mixing experiments described a few years earlier by both Helmholtz and Maxwell, and supported by the principles governing colour equations, as enunciated by Grassmann. Indeed, the Maxwell colour triangle had been described and the geometry of the triangle on the "centre of gravity" principle had been developed, while Maxwell had also given a very apt account of a three-dimensional method of specifying a colour in terms which would be very acceptable to many workers to-day.

The undue prominence apparently given to colour mixture data at that time was no doubt due to the fact that it was the chief sensory phenomenon on which fairly reliable measurements could be recorded. Three important methods of colour matching were available, namely the Helmholtz polarisation spectrometer in which the intensities of the matching stimuli were controlled by polarisation prisms, Maxwell's colour box in which slits of variable width in a spectrum provided the controls, and the colour top, in which the areas of each colour exposed on the top could be varied.

The physical energies of the red, green and blue lights used as

the matching stimuli were not known, but this was of no consequence in the development of the Maxwell triangle, since the units of the three lights were arbitrarily chosen to equalise the quantities of the three required in a match of a white light. It is rather interesting to realise that this basis for the units was almost forced on Maxwell by the lack of any other physical means of recording the intensities of the lights, and yet so effective has the system proved that it is firmly established at the present day and is embodied in the international C.I.E. system of colour specification.

This same difficulty of how to measure physical energies no doubt accounted for the absence of any measurements of the luminosity curve of the spectrum. Fraunhofer, it is true, had in 1817 published measurements on the brightness of different parts of the spectrum, but these results do not appear to have been followed up for many decades, while even at the end of the century, data were still being reported relative to the energy distribution associated with some particular light source rather than for a spectrum of known energy composition. Hence in 1868 the problem of actually sub-dividing the luminosity curve into three component parts had evidently not arisen.

Nevertheless, this was perhaps the hey-day of the trichromatic theory, when there was every promise that the main phenomena of colour vision would fit neatly into a simple framework of three independent receptor processes in the retina and three response paths from retina to brain, while the sketchy physiology of the time was simply inadequate to put the theory to a critical test. The theory, too, was well adapted to the mechanistic certainty characteristic of the Victorian era, before the subtleties of quanta, probabilities and statistics had invaded the scene.

Even so, the trichomatists were not unchallenged and in 1865, for example, Aubert's book, "*Physiologie der Netzhaut*," helped to restore the balance by the emphasis placed on adaptation and contrast phenomena, and by his insistence on four fundamental colour qualities—red, yellow, green and blue. This theme, of course, was later to be taken up by Hering, and Aubert's work may be regarded as the forerunner of the Hering school of thought. The failure on the part of the trichomatists to dissociate in their arguments the number of receptor processes from the number of distinct sensation qualities has been one of the most persistent causes of misunderstanding between the protagonists of the different theories.

What of visual physiology in 1868? Although the reddish coloration of the retina due to visual purple had been noted in the 1850s, the actual discovery of visual purple by Boll dates from

1876, with Kuhne's more exhaustive studies following during the next few years. On the anatomical side, while Treviranus had described the rods and cones in the retina in 1835, and some 20 years later H. Müller proved that the rod-cone layer was the photo-receptive layer, it was not until the 1880s that Ramon y Cajal commenced the work that was to lay the foundations of our present detailed knowledge of the retinal structures. Still more elementary in 1868 was the knowledge of the electrical response of the retina, for the first electro-retinogram had only recently been recorded by Holmgren in 1865.

Perhaps the state of colour vision knowledge at that time can best be described as lop-sided and fragmentary, a condition naturally fertile to the conflict of ideas that was so soon to develop. The cut and thrust of argument and experiment which we associate with the end of the century acquired a tempo that must have been exhausting as well as invigorating and without our Parsons' "Colour Vision" we might well despair of ever seeing the period in perspective.

We know that an extraordinary interest in defective colour vision was soon to be shown and extensive experimental data were accumulated. With the rise of the Hering school, emphasis was switched to adaptation effects and the subjective appearance of colours, but in view of the lack of information even now about the photo-chemistry of the cones, attempts to explain these effects in terms of anabolic and katobolic processes were obviously premature.

By 1924, Parsons could write ("Colour Vision," 2nd edition, p. 205): "If we rapidly survey the sections of Part I (dealing with The Chief Facts of Normal Colour Vision) we shall find that the quantitative relationships are best established for luminosity and colour with the photopic fovea and for luminosity with the achromatic eye. When we consider peripheral vision, temporal and areal effects, both for photopic and scotopic vision, the quantitative relations are far less well established. The same grouping applies to Part II (dealing with the Chief Facts of Colour Blindness)."

This, surely, could also be written in 1948. Tangible and important advances have, of course, been made in the purely physiological aspects of the histology, photo-chemistry and electro-physiology of the retina, but to what major advances can we point on the visual and subjective side? Our experimental techniques are certainly better—we have better light sources, we can measure the physical energy of our light stimulus, we have improved optical equipment such as spectrophotometers, colorimeters, colour filters, photometer wedges and filters—so that we can now control and specify the conditions of our experiments with

greater precision. This has led to more accurate colour and luminosity measurements resulting in the international adoption of standard luminosity and colour mixture data, which have in turn enabled the observing conditions of an experiment to be defined more definitely.

These can be claimed as advances, but they are technological rather than scientific, and as contributions to colour vision theory do not take us much farther than the Helmholtz-Maxwell era. Perhaps this is inevitable; perhaps we must resign ourselves to still further delay until we have more exact and direct information about the physiological processes in the retina.

In another sense, too, we have advanced. As the late Professor Selig Hecht said at the Colour Vision Conference at Cambridge in 1947, we are at last beginning to grow up. We are acquiring a confidence in our measurements that was lacking before. We no longer regard points which lie off a smooth curve as necessarily erroneous observations, but are prepared to draw curves with humps in them. We no longer regard the scatter in our observations as an annoying inaccuracy, but rather as a significant measure of discrimination ability which, when analysed statistically, may lead to useful information about the processes of discrimination.

We have a clearer idea, too, of the nature and intricacies of the subject. Mostly we remember to distinguish between the physical stimulus, the physiological reaction and the psychological sensation. Our concepts are sounder; we recognise the need to describe the conditions of stimulation and to control the observer's state of adaptation. All this is at last becoming instinctive and in this respect we credit ourselves with a superiority over our predecessors.

Yet how much of the credit should go to Sir John Parsons! In his writings and conversation he has continually reminded us that our outlook must be broad. To the physicist he has had some hard things to say. Thus in his Thomas Young Oration (*Trans. Optical Soc.*, Vol. XXXII, p. 165; 1930-31): "Physicists cannot afford to ignore the teaching of physiologists. Physicists have been and are often now supercilious of the relatively inexact sciences, such as physiology, medicine and psychology. Let them ponder upon this indisputable fact—that all their measurements are founded upon their powers of sensory discrimination. They have been let off very lightly for their comparative neglect of this fundamental fact. It is a sheer piece of luck that they quite empirically hit upon the finest of all forms of sensory discrimination, *viz.*, contour discrimination, and applied it in the form of the vernier to their instruments."

However, as the physicist is recovering from this admonishment,

he is delighted to read a few paragraphs later: "I have already criticised the failure of physicists to pay sufficient attention to physiology. *Per contra*, I much doubt if there are many physiologists who really understand the remarkable juggling feats of König, Helmholtz, Abney and other physicists."

These are pretty sharp stimuli, and if we would do honour to their author, we cannot do better than respond as he would wish. There is no very obvious sign in 1948 that all the remaining colour vision problems are about to be solved; our aim must be to fill the gaps with experiment rather than theory, and to make sure that our experiments are designed on sound principles such as Sir John Parsons would approve.

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## THE FIRST IRISH OCULAR PATHOLOGIST

Arthur Jacob—(1790-1874)

BY

L. B. SOMERVILLE-LARGE

DUBLIN

It is fitting that Arthur Jacob, the first Irish ocular pathologist, be recalled in this number of the Journal.

Although I can find no evidence in Jacob's biographies, or in his own numerous papers, that he ever actually practised any branch of medicine other than ophthalmology, he, like most of the medical giants of his age, was far from being satisfied by a mere speciality. He founded two ophthalmic hospitals, and took a leading part with others in founding both a medical school and a general hospital. He was joint founder and sole editor for 21 years of a medical journal. For 41 years he was a Professor of Anatomy and Physiology. Scientifically, he will be remembered as the first to describe the nervous layer of the retina (*membrana Jacobi*) and the rodent ulcer of the lids (Jacob's ulcer), and in the field of medical politics as a tireless fighter for medical reform, a dauntless champion of doctors' rights and a fearless opponent to all forms of quackery.

The details of his life need not detain us. Born in 1790 near the town of Maryborough (now Portlouis), in Queens County (now Leix), the son of Dr. John Jacob, surgeon to the Queens County Infirmary, and grandson of Dr. Michael Jacob (Ballinakill), he came of a stock that had been in the midlands of Ireland for some centuries. The family was English and Jacob appears to have been a direct descendant of the Jacobs who had lived in Kent in the

13th century. The Irish branch was granted land in County Wexford in 1669, and one of the family fought in the Battle of the Boyne (1690) for King William ("of glorious, pious, and immortal memory"). Arthur Jacob served his apprenticeship with his father in Maryborough and under Abraham Colles (of fracture fame), in Steevens's Hospital, Dublin, proceeding to Edinburgh to graduate M.D. in 1814. Following graduation he travelled 960 miles on foot throughout England, visiting medical institutions, and ended by crossing to France and walking to Paris. He was proud of this characteristic feat, and it is a pity he left no account of it. Napoleon's escape from Elba (1815) hastened him back to London, where he spent some months in the departments of Sir Astley Cooper, Sir Benjamin Brodie and Sir William Lawrence. By attending Lawrence's clinic at the "Dispensary for Curing Diseases of the Eye and Ear" in Charterhouse Square, later the Royal London Ophthalmic Hospital, he became the first of many Dublin oculists to enjoy the "Moorfields outlook" in ophthalmology. A personal friendship developed between Jacob and his three famous teachers, and continued until the time of their deaths, Lawrence being one of the few ophthalmologists whose work he consistently praised.

Arthur Jacob from Dublin was thus attending England's first eye hospital in the same year as were Edward Delafield and John Kearney Rodgers from New York. There is no evidence that they got to know each other, but it is at least an attractive guess and made especially so by their subsequent rôles as founders of eye hospitals.

On returning to Dublin Jacob became an anatomical demonstrator to James Macartney, F.R.S., "the greatest anatomist and physiologist that Ireland has produced," and at that time Professor of Anatomy in the University of Dublin. While there he added much to the anatomical museum which Macartney later sold to Cambridge University. It is worth noting that Jacob's work for the museum was that illustrative of the absorbent system, his interest in this if not started was no doubt stimulated by his period in London with Sir Astley Cooper, then deeply engrossed in the subject. After two years' work with Macartney, Jacob wrote his famous description of the nervous layer of the retina (1819). In 1817 he commenced clinical ophthalmic work in Sir Patrick Dun's Hospital. In 1826 he was appointed Professor of Anatomy and Physiology to the Royal College of Surgeons in Ireland, and was on three occasions elected its President. After forty-one years' whole-hearted devotion to the interests of the College he resigned, and while still actively fulfilling his professorial duties, retired to Barrow-in-Furness in Lancashire, where he died five years later.

(1874) at the age of eighty-five. He became Member of the R.C.S.I. in 1816, and in 1863 had the M.D. (Hon. Caus.) granted him by Dublin University.

#### MEDICAL FOUNDATIONS

The 19th century was in Dublin, as elsewhere, a period of hospital foundations. Seven institutions were started in the city between 1814 and 1872 for the cure of diseases of the eye. Arthur Jacob founded two of them and his son (A. H. Jacob) one. When only twenty-seven years of age, and after little more than twelve months' residence in the city, Jacob founded in Kildare Street Dublin's second ophthalmic hospital—"The Charitable Institute for the Cure of Diseases of the Skin and of the Eye" (1817). This foundation was but three years after Dublin's first ophthalmic hospital had been opened by Commander Ryall, and twelve after Mr. Saunders had founded England's first ophthalmic hospital, later to become the Royal London Ophthalmic Hospital. Jacob thus was early in the field with his first eye hospital, beating Delafield and Rodgers foundations of New York's first eye hospital (the New York Eye Infirmary) by three years. The "skin" side of the institution was not handled by Jacob but by his dermatologist chief Professor Macartney, and was discontinued after a few years when the name was changed to "The Institute for the Cure of Diseases of the Eye." In the same year, 1817, Jacob and Macartney were "given permission to see eye and skin cases respectively in one of the empty wards" of Sir Patrick Dun's hospital. This appears to be the first purely ophthalmic appointment to a general hospital in Dublin. Jacob carried out operations for cataract in his Institute, but does not appear to have done any teaching there. He closed this hospital after six years to found, with the great Dr. Graves and others, the Park Street Medical School. This became one of the most famous of Dublin's private Medical Schools. A contemporary account of the school from the *Lancet* of 1825 on the occasion of Jacob's giving the opening lecture recalls it vividly: "Tossed to and fro, like a ship in a gale, we ascended to the theatre, and soon found ourselves seated amidst a dense multitude, where we could easily perceive that neither elbow room nor liberty of conscience was to be expected . . . a neat theatre, originals and imitations both in abundance; here lay a fish that would have made a gourmand's teeth water; there a copper-plate, almost making the shadow as real as the substance itself; while between them rose skeletons in the naked majesty of bare bones and pride of varnish."

Jacob left Park Street Medical School two years after its foundation on his appointment of Professor of Anatomy and Physiology



to the R.C.S.I. (1826). In the same year he was elected to the full staff of Sir Patrick Dun's Hospital, which post he retained for the next 27 years. As, however, this hospital was wholly medical and as Jacob's appointment was a "surgical" one, it is unlikely that he did more than act in a consultant capacity—and perhaps see out-patients there. Certainly three years after his appointment he founded his second eye hospital—"The Ophthalmic Hospital," 1829, in Pitt Street (now Balfe Street). Here Jacob gave "clinical instruction" and "taught operations" for the modest fee of three guineas for three months. This little hospital was maintained and run solely by Jacob and has the distinction of being the only hospital in Dublin that during its entire existence was exclusively devoted to diseases of the eye. After some years as Professor of Anatomy and Physiology, Jacob, feeling the College was handicapped by the fact that many of the Staff were unattached to any teaching hospital, joined with his colleagues as the prime mover in the foundation of the City of Dublin Hospital (1832). There he had beds and taught clinical ophthalmology for twenty-four years. This, the last of his foundations, was the only permanent one and remains to-day as "The Royal City of Dublin Hospital." On its opening Jacob closed his Ophthalmic Hospital in Pitt Street.

#### MEDICAL EDITOR

Jacob's contribution to foundations for the practising and teaching of ophthalmology, extensive as they were, are overshadowed or indeed wholly forgotten by his work as a fighter for medico-political reform. He became in 1837 assistant editor to the Dublin Journal of Medical Science but had to relinquish this post probably due to his personal attacks on medical colleagues. Two years later he founded with Henry Maunsell the "Dublin Medical Press," and remained its editor and inspiration for 21 years. This Journal later moved to London, and it still flourishes under the changed name of "The Medical Press and Circular." Although we know that robust language was at that time common in medical controversy, the force of Jacob's editorials and medico-political articles make strange reading to us a century later. He assails a professorial rival with "the chronic medico-literary diarrhoea under which the learned Professor has so long laboured," "the heterogeneous discharges with which he inundates the journals," "the foetid ichor which distills from such a quill." The editor of the Lancet (1841) is no less outspoken. "Messrs. Jacob, Maunsell, Porter, all the rag, tag and bobtail of the College School, hatched in corruption, though they still linger about the dunghill that gave them birth." In the heat of medico-political conflict to-day it is

well to remember that our medical forebears thought equally strongly a century ago. It is also of interest when reviewing the momentous medical changes of to-day to recall that Jacob in "The Medical Press," although strongly advocating the central control of local charities was anxious to retain the element of "charity," and foresaw danger in establishing a "centralised iron-bound medical service." The Medical Press keenly supported the Medical Act of 1858, but resented the improved status it gave to apothecaries. All Jacob's fights for reform were for his profession and his College. He took up arms immediately if he considered that either were attacked or the smallest disrespect shown to them. Any suggestion of professional quackery or advertisement called forth his most vitriolic utterances, and amongst these he powerfully denounced the practice of "going snaeks," the attractive term then used for what we now call "fee splitting." In 1839 he went so far as to print a list of doctors, many of them high in the profession, whose names appeared in commendation of proprietary articles. His literary output was immense. During the 22 years of this editorship none of the weekly editions of the Dublin Press failed to carry something from his pen. Jacob's medico-political speeches and papers, though perhaps failing from their very vehemence to carry conviction, can certainly never be said to make dull reading.

#### MEMBRANA JACOBI

Jacob read his "Account of a Membrane in the Eye" before the Royal Society in 1819. At that time anatomists described the retina as consisting of two parts, "the medullary expansion of the nerve, and a membranous or vascular layer," the former being



"Membrana Jacobi"—the figure illustrating Jacob's original description in the eye of a sheep—*Philosophical Transactions*, 1819.

next the choroid and the latter next the vitreous. Jacob wrote: "It is not the nervous layer which I detach . . . because I leave the retina uninjured." Again he states that this membrane "besides being attached to the retina is also attached to the choroid coat." He therefore considered it to lie between the choroid and the retina. What, however, he described and illustrated and what is named after him, "*membrana Jacobi*," is not the retina but what we now know to be only its neural layer. If we were to replace the inaccurate clinical term "detachment of the retina" by "detachment of Jacob's membrane" we would be anatomically correct. To the end of his life Jacob himself never seems to have realised the true nature of his important discovery.

His method of demonstrating this membrane was to fix the posterior half of the eye to a piece of glass covered with an inverted glass sphere, the whole was filled with water so that the eye floated and the sphere acted as a magnifying glass. The preparation was then capable of being passed around the class for examination. That it was not wholly successful is suggested by the semi-serious account of one of Jacob's students in the Park Street Medical School (*Lancet*, 1825). "In some papers published in one of the periodicals, Jacob lays claim to the discovery of an undiscovered something in the eye; but not a creature we believe gives credit to the assumption. We were ourselves present when he attempted to describe this 'mare's nest,' but neither we, nor any of those around us, could see the imaginary creature." However, the anatomical world could see the "imaginary creature," and Jacob's discovery had world wide recognition.

His anatomical dissections of the eye were very delicate, and in a period with few optical aids it is intriguing to consider what part his undoubted myopia may have played both in these and in his interest in the study of the minute. In 1823 he read a paper entitled, "Inquiries respecting the Anatomy of the Eye," before the Medico-Chirurgical Society of London. Here he described and produced illustrations of the *membrana pupillaris*. In one case that he illustrated he had succeeded in injecting a single vessel of this membrane at the 9th month of gestation. His observations led him to refute the then prevailing theory (of Blumenbach) that this membrane disappeared by a rent taking place in its centre and the vessels contracting to the iris, his contention being the now accepted one that the membrane "loses its vascularity, becomes exceedingly thin and is finally absorbed." By removing the cornea he demonstrated what we now know as Descemet's membrane to have no resemblance to the cornea itself ("no two membranes can perhaps be more dissimilar") but to be of "precisely the same nature as the capsule of the lens."

He left his entire anatomical museum containing some beautiful paintings of the iris on ivory to the R.C.S.I.

### JACOB'S ULCER

"Observations respecting an ulcer of Peculiar Character which Attacks the Eyelid and Other Parts of the Face" appeared in the Dublin Hospital Reports for 1827. Here Jacob describes with



"Jacob's Ulcer" and Jacob's cataract needle, from the original illustration. (*Dublin Hospital Reports*, 1827).

comprehensive accuracy the condition now known as rodent ulcer (Jacob's ulcer). Time has added little to his original description, "the characteristic features of this disease are the slowness of its progress, the peculiar condition of the edges and surface of the ulcer, the comparatively inconsiderable suffering produced by it,

its incurable nature unless by extirpation, and its not contaminating the neighbouring lymphatic glands." He mentions local and general treatment only to condemn them, and his finding that early surgical removal offered the only hope of cure held for the best part of a century. Jacob was jealous of this paper and never failed to draw the attention of subsequent "discoverers" of this ulcer to it.

#### AS A SURGEON

As a surgeon Jacob is best remembered by his treatise on "The Removal of Cataract as Performed with a Fine Sewing Needle through the Cornea." Although this was published in 1850 he had previously written both of his cataract needle and the operation he recommended in 1827 (Dublin Hospital Reports). The needle is an ordinary round sewing needle (No. 7 in size), bent at the point. This bending Jacob did himself, and he states that five or six needles in a hundred would stand the bending without breaking. Makers' attempts to reproduce his needle he despises—however, it is illustrated in Weiss' catalogue of 1865—and he recounts in detail both how to bend it and how to fit it to a handle. Of the value of both needle and operation he is characteristically dogmatic. He writes that some despise the needle "because it has not the imposing appearance of a finely polished blade with ivory handle and silver ferrule," but warns those "fond of improving surgical instruments to suit their peculiar notions" that it must be exactly to his specification. He concludes, "of the superior qualities of this needle I have not the slightest reason to change my opinion. It is, I am satisfied, by many degrees the best for the purpose." Alas that time has proved him wrong. Of the operation for cataract extraction, then coming into vogue, he states that although "malicious persons will say that I advocate this operation (of needling) because I cannot perform that of extraction," it is "on account of its hazardous nature a disgrace to surgery." Few of us would disagree with him in those pre-anaesthetic days.

His dramatic description of an eye operation as carried out 120 years ago, recalling as it does so clearly the character of the surgeon, must be given in his own words. "I seat the patient in a chair and make him sit straight up or inclining, according to his height. If very tall I raise myself by standing on a large book or two, or on anything which answers the purpose to be found at hand. In my own place of business I find old medical folios answer the purpose well; operating chairs, although very imposing and calculated to produce effect, I have not adopted, not finding myself at ease with such things. When he is seated I lay the patient's

head against my chest, and placing the middle finger of my left hand on his lower and the forefinger on his upper eyelid, and gently holding the eye between them, I strike the point of the needle suddenly into the cornea, about a line from its margin, and there hold it until any struggles of the patient, which may be made, cease. There must be no hesitation here, for if the cornea be touched without fixing the point of the needle in it, the eye will turn rapidly and the surface will be scratched. I advise the operator to pause here for a moment, holding the eye firmly and steadily on the point of his needle, and if necessary to say a word of encouragement or remonstrance to the patient." How vividly one sees the patient "struggling" on the point of the needle while seeking composure through the surgeon's "words of remonstrance." Jacob broke the lens up strongly, and he states that absorption took place remarkably quickly, patients sometimes being able to read within ten weeks. It is interesting to note that he cites the frequent occurrence of post-operative vomiting lasting often for 24 hours, and attributes it to the action of the broken lens on the iris. Jacob did not coddle his patients, "the less of bed the better, and the sooner the drawing room is made the place of convalescence, the better also." Whatever time may have decreed in respect to his needle and operation, we can endorse his conclusion, "the truth, perhaps, has never been told with respect to the result of cataract operation and perhaps never may be told."

Jacob has left us accounts of two other operations—for trichiasis and entropion. That for trichiasis appears to be original, although perhaps the credit should go to the patient. He "drilled a needle into the root of the inverted eyelash and then held a lighted taper to it until the part into which it was inserted was burnt to whiteness." For entropion he advocated the horizontal splitting of the tarsus and then everting it with sutures as described by his contemporary, Sir Philip Crampton. Jacob vividly demonstrated one such case pre-operatively to his students, "observe her scalded turned-in lids, depressing countenance, with profuse tears warning me that I have to encounter a struggle in which physical force must be relied on more than persuasion." No wonder.

Jacob was a conservative surgeon. He disapproved of paracentesis (for inflammatory conditions), and strongly criticised iridectomy, an operation he never seems to have carried out. For the "muscle-cutting candidates for fame" he had nothing but scorn, assisted perhaps by the fact that Sir William Wilde wrote approvingly of it. In acute dacryocystitis he recommended opening the sac through the conjunctiva rather than through the skin.

## VARIOUS PAPERS

In 1843 Jacob criticised "an attempt to make the study of pathology into a distinct department . . . but why or wherefore no one can tell . . . it is the province of the anatomist, physiologist, the teachers of medicine and surgery and the clinical teacher." However, he not only was zealous in carrying out post-mortems, but in 1846 wrote a long paper entitled "On Diseases of the Eye as a Guide in the study of Pathology." In this he points out that due to the transparency of the cornea, the exposed condition of the conjunctival vessels and the easily seen delicate iris tissue, morbid processes are well observed and studied in the eye. In these, he writes, the "accurate observer has living proof of what he supposes may be going on in other places under similar circumstances, but which he cannot demonstrate until death enables him to expose the parts." A century later we find ourselves returning to Jacob's pathological concept of the living tissue undergoing morbid changes.

In the "Cyclopaedia of Practical Medicine" (1834), Jacob contributed long articles on "Ophthalmia" and "Amaurosis." When considering "Egyptian Ophthalmia" he mentioned that so heavily infected were the troops lately returned from the Middle East to Ireland that a special ward was opened for them in Steevens' Hospital under Mr. Colles. On "Amaurosis" he contributed over 18,000 words, and it must seem strange to us, living in an age that takes for granted visual examinations of body cavities, that neither here nor in his account of the membrane that bears his name, nor in his writing on retinitis, did he ever consider the possibility of actually seeing the fundus of the eye.

Helmholtz made his fundamental discovery in 1850 and Jacob's contemporary in Dublin, Dr. H. Wilson (the natural son of Sir W. Wilde), published his book, "Theory and Practice of Ophthalmoscopy" in 1868, yet I can find no suggestion that Jacob himself ever saw the ocular fundus. His first comment on the ophthalmoscope was in 1855, "not one man in 20 will be able to manage this instrument," and a year later he writes, "all we ask about the ophthalmoscope is that performers on it will not require us to believe all they say as to what they see through it." Jacob's famous rival, Sir William Wilde, showed an equal lack of enthusiasm, and he also never appears to have seen the human fundus.

In 1848 Jacob published his only book, "A Treatise on the Inflammation of the Eyeball." In spite of Mackenzie's classical text-book this uninviting, poorly printed, unillustrated pocket-sized volume seems to have had a real popularity in Dublin. There is reasoning in it beyond its time. Jacob repeatedly insisted that in

"iritis" all the uveal tract must be considered to be involved. He denounces wholesale cupping and, in opposition to Mackenzie, denies that inflammation takes place in the lens. He draws attention to social conditions among the poor ("badly fed, improperly clothed and miserably lodged") as a cause for ocular inflammation. And flies in the face of accepted custom by criticising the well to do who follow "the usual unhealthy practice of sleeping in a bed hung round with curtains to exclude light and confine foul air," in bedrooms, "more like the crowded storerooms of furniture dealers than apartments provided for human beings." Jacob would assuredly be in the forefront of social medicine to-day.

Jacob's mechanical bent is shown by a paper on a "Proposed Improvement in the Construction of the Cistern of the Portable Barometer" (1826). Instruments incorporating this suggestion were constructed. He also wrote and illustrated "A Description of an Apparatus for Injecting the Absorbent Vessels" (1825), a mechanical problem that intrigued him for many years. Comparative anatomy always interested him. One summer he heard that a dead whale, found floating off the West coast of Ireland, had been seized by the officers of the Admiralty. Although "probably six weeks dead and the weather being warm it provided a most uninviting subject for dissection"—he dissected it while floating and brought back specimens for his museum. Another time he made haste to buy a whale that had been washed ashore on Killiney Strand, near Dublin, and dissected it there. He wrote on the "Intra-orbital Cavities in Deers and Antelopes," on "The Mammary Gland in Cetacea" and on Sun Fish, as well as accounts of these whales.

Jacob was so keen a clinical observer that one is hardly surprised to find him passing beyond the merely physical. In a long paper with a resounding Victorian title, "An Essay on the Influence of the Imaginations and Passions in the Production and Cure of Diseases" (1823), he embarks on psychology and boldly advocates "that the power of the imagination and passions extensively influences the ordinary operations of the animal economy, and that the same influence is not only capable of producing diseases but of contributing to their removal." We are only now commencing to realise the truth of his assertion—"I fear, however, that our knowledge of the animal economy is far too limited to enable us to decide what diseases may or may not admit of cure from an impression of the mind." It is characteristic of Jacob's scientific approach that, unlike most of his medical contemporaries, he is not prepared just to sneer at the cures that he quotes in this paper as resulting from charms, amulets, and such like, but is prepared to give the whole subject serious consideration. This interesting



contribution is a clear call, made 120 years ago, for psychological investigation.

### THE MAN HIMSELF

Arthur Jacob lived in a large five-storied Georgian house in Ely Place (No. 23)—a quiet street of good houses and wealthy inhabitants. His house was half way between his two centres of interest—his hospital (The City of Dublin) and his College (The Royal College of Surgeons), a pleasant walk of half a mile from each. No doubt this assisted him in his almost invariable custom



Arthur Jacob's house—23, Ely Place.

of commencing hospital work at 8 o'clock in the morning. All his life he was a man of great physical energy, nothing else could have permitted him to get through his hospital work, his "punctual and energetic professional duties," "his extensive private practice," and his large weekly literary output. His son tells us that his custom was to retire to bed after dinner (a 6 o'clock meal in the Victorian era), for a few hours' sound sleep, then to arise and "after tea" to spend most of the night reading and writing. Dr. Van Loon, physician and friend to the artist Rembrandt, is stated to have said that he could judge of a patient's character by the books at his bed side. Jacob's library of some 1,500 books he left to his college. It is not all composed of scientific volumes. There are also many books of travel (although once settled in Dublin Jacob never seems to have gone farther than London and that only very seldom), and many on the scientific aspects of agriculture (although as far as we know he never farmed), but perhaps stranger still are numbers of volumes of poetry, including the *Odyssey* and the *Iliad*. Something can surely be judged of a man by the library he makes, and on this assumption a surprisingly gentle side of Jacob is revealed.

The photograph reproduced is from a portrait done when Jacob was in the middle thirties. The *membrana Jacobi* was discovered, and Jacob's ulcer described. He sits at the corner of a table, sleeves rolled back, scalpel in hand, just about to divide an eye and mount it under the glass sphere that stands ready—thus to demonstrate his discovery. In the official portrait of him painted 35 years later for the Royal College of Surgeons he sits in much the same position in a similar chair at the corner of a similar table, his hair still curls and his very spectacle frames seem similar, but the face is lined and stern and the attitude uncompromising. At about the period of the younger portrait he is described by one of his students: "A gentleman of duodecimo stature so neatly habited that the affectation of the simplex munditiis could not disguise the assured indifference to toilet arrangements and exterior appearances. He was harnessed in a pair of spectacles so admirably fitted . . . that one might have mistaken the whole optical apparatus as the natural production of the parts . . . over the springs of this beautiful piece of mechanism hung two luxurious ringlets of beautiful auburn hair. . . . Around the medley of organs . . . there breathes a halo of kindness and conciliatory effulgence of good nature." We must agree that this account suits the portrait, but as the years passed much of the "halo of kindness" passed also, and he became as brusque and cantankerous in his manner as he became intolerably critical in his writing. Of a retiring disposition, a burner of the midnight oil and one who shunned even

the mildest convivialities, Jacob was undoubtedly an introvert. Although his aloof manner may have denied him many personal friends, his unselfish character earned him a score of sincere



Arthur Jacob—circa 1830.

admirers. He suffered from an ever present fear of showing the smallest suspicion of self-aggrandisement. This, as well as his intolerance of manner, is seen in his retort to the friends and colleagues who sought to honour him by a presentation. Knowing his feelings in this matter they were at some pains to decide on

something that he might accept. Finally, a medal was decided upon with Jacob's portrait on the obverse and suitably inscribed on the reverse. A gold one was struck for himself, a silver one for his brother (Dr. John Jacob of Maryborough), and bronze ones for the members of the presentation committee. These completed, the committee waited on the professor to request his acceptance (1860).



The Medal presented to Arthur Jacob.



Arthur Jacob's ink-bottle.

His reply is quoted by his son in "The Medical Press" (1874)—"I cannot accept of this or any other testimonial, but if at my death you still think that I deserve it, you may nail it on my coffin." History does not relate how he was persuaded, but persuaded he was, and a year later he attended a dinner held in his honour at the Royal College of Surgeons, when the medal was formally presented to him. His portrait was also ordered to be painted by the Council, and it hangs there to-day in the Examination Hall. His bust, too, is granted an honoured place in the college.

There is, however, another more personal reminder of Arthur Jacob's 44 years' work in the college. It is a mis-shapen penny ink bottle now mounted in silver and with an inscription which tells us it was his. If it shows the parsimonious character of the user it also shows the sincere respect of those that came after him. Men only do these things in memory of those they honour.

Jacob married Miss Sarah Coote Carrol in 1824, the same year as the Park Street Medical School was founded. He had five sons. The eldest (John Alexander) went into the church, the second (Samuel) became an oculist in Melbourne (Australia), the third (Arthur) was a civil engineer in Bombay and later in Barrow-in-Furness, the fourth (Archibald Hamilton) succeeded his father as oculist in Dublin and editor of "The Dublin Medical Press," and the fifth became an engineer in Travancore, S. India.

There can be no doubt that the ophthalmological tragedy of the 19th century in Dublin was the personal animosity of Arthur Jacob and William Wilde. Two dominant, energetic, and essentially intelligent men of wholly different character. The Wildes, Sir William, Lady Wilde (Speranza) and their son Oscar were spectacular extroverts. Wilson has shown us that Wilde himself was a *bon viveur*, kept a generous table, and rejoiced in the company of authors, scientists, nobility and peasants alike. He was 25 years younger than Jacob and died but two years after him, so that during almost his entire active life Jacob edited "The Medical Press." Yet the older ophthalmologist hardly ever mentions his brilliant young contemporary, and then only to condemn his work. Wilde writes a long, detailed, and most instructive report on the condition of the "Union Poor House Hospital" in Tipperary. This calls forth from Jacob an editorial headed sarcastically "Wilde's Pastoral," severely critical because Wilde outlines the treatment of ophthalmia to the local medical officer and thereby offends Jacob's idea of professional dignity. Again an American doctor visits European clinics and Jacob sneers, "in Dublin he is sure to dine with Dr. Stokes and sup with Surgeon Wilde." (We cannot refrain from envying this American wanderer). He never

mentions the internationally known eye hospital (St. Mark's Ophthalmic Hospital), founded and run by Wilde, nor does he give any notice to Wilde's innumerable scientific articles. Wilde, when editor of "The Quarterly Journal of Medical Science," deals more kindly with Jacob "if we were writing as historians simply and not in our editorial capacity; we might offer some remarks of the tone and style of 'The Dublin Medical Press'—but under existing circumstances we deem it more proper to refrain."

For forty years these two men dominated the ophthalmology of Dublin, and who can doubt that had they but combined in its organisation and scientific advancement the gain to the nation's medical life would have been great indeed.

Without the enthusiastic assistance of Professor Widdess, M.A., Librarian and Lecturer in Biology at the Royal College of Surgeons in Ireland, and of Miss O'Brien, Assistant Librarian at the Royal College of Surgeons, the writing of this paper would not have been possible. To both I tender my sincere thanks. I am also indebted to Prof. Moorehead, who very kindly advised me over Jacob's association with Sir Patrick Dun's Hospital. Dr. Greene, of Norwich, a descendant of Arthur Jacob's was good enough to supply me with the photograph of Jacob's portrait that is in his possession. Mr. W. R. Jacob (London), Mr. R. F. West (London), Mr. Prior-Kennedy (Darlington), and Mrs. Kennedy (Tullamore) have all put me in their debt by personal communications on their ancestor. I am greatly obliged to Miss Thompson who went to much trouble to produce these excellent photographs.

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RADIOTHERAPY OF MALIGNANT INTRA-OCULAR  
NEOPLASMS

BY

H. B. STALLARD

LONDON

THE value of radiotherapy for glioma retinae is established. This tumour is very radiosensitive and when a quadrant or less of the retina has been affected by the growth treatment by radon seeds has caused the tumour to disappear and in a series of such cases treated at St. Bartholomew's Hospital there has been no recurrence in a period of follow-up from 1929-1948.

The results in the treatment of malignant melanomata by radon seeds are less fortunate. Metastatic carcinoma of the choroid is very radiosensitive and in some such cases it may be justifiable to use this treatment to conserve a little vision or to lessen the misery of the remaining months of the patient's life.

We have tried to strike the neoplasm with a dose judged to be adequate for its destruction without producing irremediable damage to the eye, and to bring the source of irradiation as close to the tumour as it is possible to obtain by surgical exposure. The insertion of a radon seed through the sclera into the growth has been abandoned for the technique of suturing radon seeds to the sclera over the site of the neoplasm, and we are now making trials with plaques of either platinum or silver 0.5 mm. thick containing radium salt and curved to fit the sclera neatly over the site of the neoplasm and fixed by sutures passing through holes in the edges of the plaque and thence through the superficial layers of the sclera. The advantage of these will be a more even and accurate distribution of irradiation than is the case with a straight radon seed fixed at a tangent to the surface of the sclera, and a source of supply which remains constant and is available for immediate use for owing to labour difficulties there is in England to-day a delay up to 10 days in obtaining radon seeds.

The transparency of the eye media affords us special opportunities in this work of assessing the exact size of the neoplasm, of marking its boundaries by surface diathermy coagulation at operation and of following up its subsequent behaviour.

## DOSE

For the permanent arrest and destruction of a malignant neoplasm it is necessary for the whole tumour-bearing area and indeed the tissues wide of this to receive a uniform intensity of irradiation effective for the particular growth during the whole time

of the treatment. In the absence of accurate knowledge as to the exact dose that the tissues receive it is safer to give the maximum dose that the tissues will stand without incurring the risk of serious destructive changes and complications. A sub-lethal dose may inhibit the neoplasm for a period of time but it inevitably recurs and the success of further radiotherapy is jeopardized. It is therefore necessary to arrange the radium or radon in such a way as to produce an adequate intensity and homogeneity of irradiation.

Gamma ray therapy is measured in terms of the ionization in the air by the radiation, and such measurements have been taken in post-mortem material using small Sievert condenser ionization chambers at various sites in a new growth which had been subjected to interstitial radiotherapy. The unit of intensity has been defined as "the intensity of the radiations at a distance of 1 cm. from 1 mg. point source of radium element (in equilibrium with its products) filtered by 0.5 mm. of platinum." One curie of radon is the quantity of radon in equilibrium with 1 gramme of radium and 1 millicurie is one-thousandth part of the this. The millicurie-

hour intensity (I) is given by the formula 
$$I = \frac{m}{r^2} \times 1 \text{ mc.}$$
 r is the

distance in centimetres of the treatment point from the source and m is the strength of the radon source in millicuries.

"The roentgen is the quantity of x (or gamma) radiations which, when the secondary electrons are fully utilized and the effects of all scattered radiation avoided, produces in 1 c.c. of atmospheric air at 0°C and 76 cm. mercury pressure such a degree of conductivity that 1 electro-static unit of charge is measured under saturation conditions."

From practical experience to date it seems better to use radon seeds as close to the neoplasm as possible in the treatment of malignant intra-ocular tumours rather than the employment of massive doses delivered from radium needles set in plaques or the radium "bomb." Such large doses in most cases have had a destructive effect on the eye, at the worst causing its loss through corneal necrosis and panophthalmitis. Depilation of the lashes and eyebrows, a burn of the conjunctiva and irradiation cataract are lesser ills.

To-date the number of cases of malignant intra-ocular neoplasms in which radiotherapy was considered justifiable have been too few and the dose tried too empirical and experimental to give as yet definite advice on this point. As a temporary guide it seems that a dose of 3,500 r is adequate to destroy glioma retinae occupying one quadrant of the interior of the eye.



At present (1948) radon seeds 1 and 2 mc. are used and these are stitched to the sclera at appropriate sites in the case of intra-ocular neoplasms. Their active length may be varied up to 6 mm., their diameter is 1.4 mm. and the screen is 0.5 mm. of platinum.

The radioactivity of radon is reduced to half in 3.86 days, to one-fifth in 8.8 days, and at the end of 40 days only 0.07 per cent. remains. This decay factor is constant. One millicurie is destroyed in 133 hours. The seeds are left in place 4 to 8 days depending on the dose required.

I am grateful to Mr. F. S. Stewart, Radium Department, St. Bartholomew's Hospital, for the following description of his findings and for his help and ingenuity in designing a new radium applicator for the eye.

A review has been made of 22 cases successfully treated at St. Bartholomews' Hospital by radon seeds, in order to form an estimate of the radiation dose received at various points. In Table A the cases are arranged according to the size of the glioma. The dimension listed as "diameter" is measured along the spherical surface of the retina; the height is measured from the level of the retina and is an estimate since accurate measurement of this dimension is impossible.

TABLE A  
*Radon Treatment of Glioma Retinae.*

Size of Growth		No. and Strength of Radon Seeds (applied 168 hours)	No. of Cases Treated	Dose at Apex of Growth	Minimum Dose in Region of Tumour, at a level 1 mm. inside surface of Sclera
Diam. mm.	Height (Estimated) mm.				
3	2.5	1 × 2 mc.	4	8800 r	23400 r
		2 × 1.1 mc.	2	9050 r	22600 r
4.5	3	1 × 2 mc.	1	7050 r	15700 r
		3 × 1.1 mc.	1	10900 r	30200 r
5	3.5	1 × 2 mc.	5	5800 r	13900 r
7	5	1 × 2 mc.	4	3500 r	9550 r
		2 × 2 mc.	1	6300 r	12900 r
8	5.5	1 × 2 mc.	1	3350 r	7600 r
10	7	2 × 2 mc.	2	4350 r	8500 r
21	13	4 × 2 mc.	1	2900 r	12300 r

In all cases treated with 2-mc. seeds:—

	Where 1 Seed Used	Where more than 1 Seed Used
Maximum Dose at a level 1 mm. inside surface of Sclera	38500 r	50000 r
Maximum Dose where seeds touch Sclera	125000 r	150000 r

The lowest dose received by any part of the tumour is at its apex and the value calculated is governed mainly by the figure estimated for the height. The apex doses shown are therefore only approximate, but they indicate that the smaller growths have generally received considerably higher doses than the larger. The fact that 7 successful results have been obtained with minimum tumour doses of 3,500 r or less suggests that the amount of radon could safely be reduced for diameters below 7 mm.

The dose received by the base of the glioma will, strictly speaking, depend on the combined thickness of sclera, choroid and retina at the site in question, but for simplicity the doses shown for the base are all calculated for a spherical surface 1 mm. inside the outer surface of the sclera. The dose at this level is very uneven due to the proximity of the seeds and reaches a maximum of 38,500 r in cases treated by a single 2-millicurie seed and approximately 50,000 r where several seeds were used. The minimum dose within the area of the dose is in most cases 9,000 r or more, as shown in Table A.

It is of interest to note that the outer surface of the sclera in direct contact receives as much as 125,000 r in single-seed treatments and 150,000 in multiple-seed treatments.

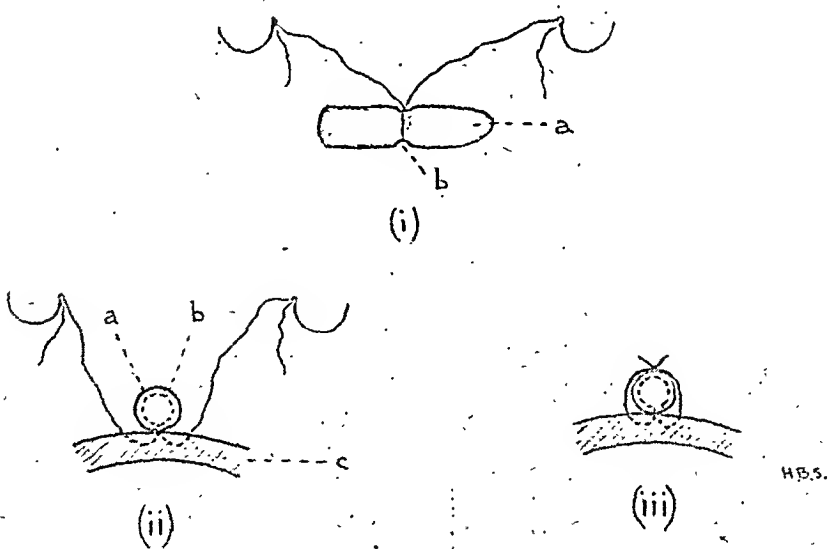


FIG. 1.

Diagrams drawn to show the method of suturing a radon seed to the sclera. (i) *a* Radon seed; *b* Fine black silk thread tied in a groove filed through the platinum envelope circumferentially about its centre. Arterial needles are attached to the free ends. (ii) The interrupted line represents the silk thread running in the groove around the radon seed and then passing through the superficial layers of the sclera, *c*. (iii) The ends are brought together over the seed and tied in the groove.

## TECHNIQUE

In 1929 Foster Moore inserted a radon seed into an intra-ocular neoplasm through a scleral incision made with an angular double-edged knife the exact width of which equalled the diameter of the radon seed. The point of the knife entered the base of the neoplasm and on its withdrawal a radon seed in a special holder was introduced point first into the incision. In the case of malignant melanoma of the choroid the solid growth was apt to be pushed on in front of the blunt tip of the radon seed. Fig. 1 shows the

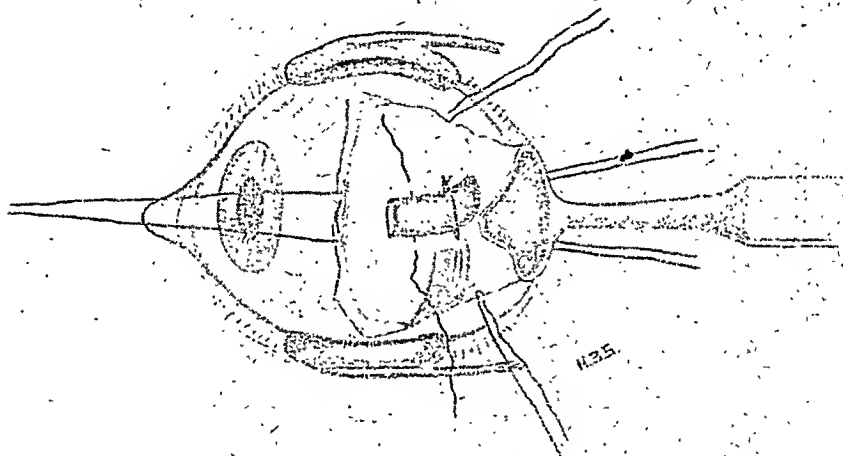


FIG. 2.

Glioma retinae of left eye at the temporal edge of the optic disc. The external rectus has been divided and the inferior oblique exposed. A stent strip moulded to the sclera and containing a 2 mc. radon seed is applied and held in place by two sutures.

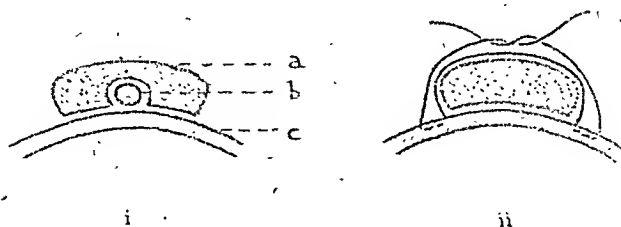
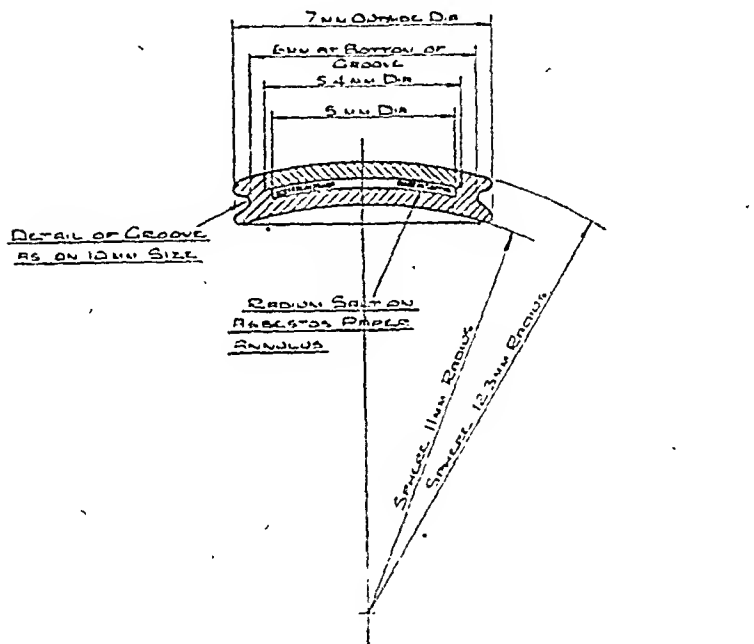


FIG. 2A.

i. Cross section through end of strip of stent holding radon seed; (a) Strip of stent dental wax moulded to sclera; (b) Radon seed embedded in stent; (c) Sclera. ii. Method of suturing stent strip to sclera in front of and behind equator.

technique I have used for suturing a radon seed to the sclera, and Fig. 2 that of suturing to the sclera a stent strip, with an embedded radon seed, or 2 seeds, so that the radon lies close to the optic nerve sheaths at a point where suturing the seed directly to the sclera affords considerable technical difficulties.

Fig. 3 shows a shallow platinum or silver radium container 0.5 mm. thick curved to fit the sclera and sewn to it.



Sectional view of eye applicator 5mm. in size.

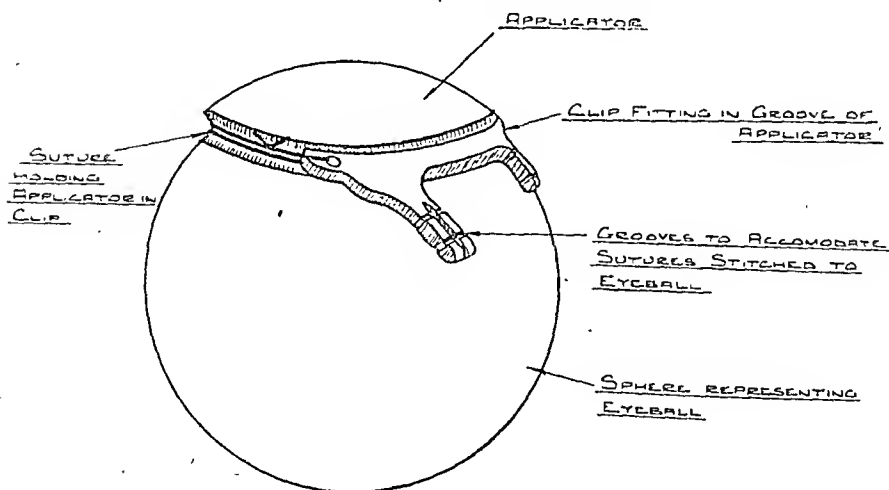


FIG. 3.

Radium applicator for attachment to sclera.

## REACTION OF GLIOMA RETINAE TO RADON

About the third day after the application of radon, parts of the neoplasm, particularly at its periphery, become more densely white. The appearance is comparable to flakes of curdled milk,

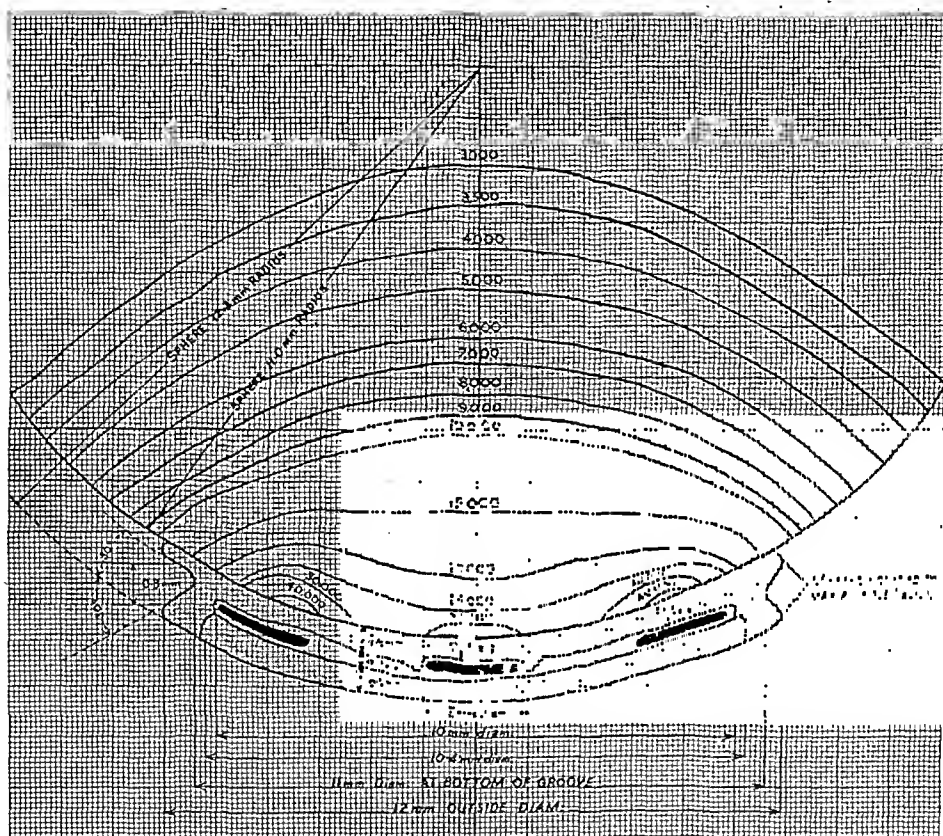


FIG. 4.

the glioma retinae looking like flocculent cream cheese in its pre-operative state. In one or two weeks some of these dense white flakes become separated from the main mass of the neoplasm and the majority remain suspended near it. Rarely does such a flake gravitate in the vitreous to a place remote from the neoplasm, where it ultimately becomes absorbed.

Shrinkage of a successfully irradiated neoplasm is chiefly evident in the second and third week and continues till the eighth to tenth week. The periphery of the neoplasm is the first to be absorbed.

There may remain at the centre some greyish-coloured degenerative material for several months in cases where the neoplasm occupies about a quadrant of the globe. The scar at the site of application of a radon seed is characteristic (Fig. 5). It is flat, has a crenated edge fringed with pigment, and the centre is dense



FIG. 5.

Glioma retinae. Right eye. Mass in upper nasal quadrant has been successfully irradiated. The scar in the retina and choroid is characteristic of an irradiated area. It has a crenated pigmented edge and the adjacent fundus shows fine pigment stippling. The retinal vessels are occluded in the upper nasal quadrant and some greyish exudates are around the macula.

white. The surrounding fundus is finely stippled as if peppered with pigment. The retinal vessels in the region of the neoplasm are occluded.

These changes are produced at the site of application of the seed. In a case of glioma at the left macula a 2 mc. radon seed was purposely placed away from the macula at the equator in the 2.30 o'clock meridian. The neoplasm disappeared from the macula leaving only a faint greyish discoloration, which was indeed difficult to detect in comparison with a normal fundus, whereas the site of application of the radon seed showed the characteristic changes described above and shown in Fig. 5. In the case of a large neoplasm a second application of radon may be necessary, but it is as well to wait for at least three months after the first application before deciding on this course.

For a description of the effects of radium on other ocular structures the reader is referred to Radiant Energy. (*Brit. Jl. Ophthalm.*, Monograph Supplement, 1933.)

#### RADIUM APPLICATORS

The use of radium in place of radon would be advantageous in avoiding the delay incurred in the preparation of the radon seeds. The conventional form of radium needle is, however, far too long for use in a similar manner to the seeds and it is proposed to use a new type of radium applicator as described below.

These applicators (see Fig. 3) have a platinum casing in the form of a segment of a spherical shell 1.3 mm. thick, the inner radius of curvature being 11 mm. to allow the device to be applied closely to the sclera. The casing is hollow, with a wall thickness of 0.5 mm., leaving a cavity 0.3 mm. in width. A range of sizes of applicator suitable for irradiating circular areas of the retina from 2 to 20 mm. in diameter is proposed, and according to the area to be irradiated, the cavity contains an asbestos paper disc or annulus (or both) impregnated with radium salt. The wall thickness of the casing is sufficient to absorb all alpha and beta radiation so that the irradiation is purely by gamma rays.

The applicator is secured by sutures to the sclera. A groove is made on the edge of the casing and a semi-circular clip, with projecting lugs which can be sutured to the sclera, is made to fit the groove. Several interchangeable clips of different lengths are made for each applicator so that the sutures can always be made near the equator, no matter in what part of the globe the glioma is situated.

The radium loading has been calculated to give a dose of approximately 3,500 r in one week (168 hours) at the apex of the growth. (For this purpose, the height of the glioma has been assumed to be seven-tenths of the diameter.) The distribution of the radium

over the surface treated has been chosen so as to make the dose as uniform as possible at the surface of the retina. Taking the 10 mm. diameter as an example, the dosage distribution is as shown in Fig. 4.

[The applicators are made by Messrs. Johnson, Matthey and Co., Ltd., to whom acknowledgment is made for collaboration in the technical aspects of the design.]

#### CLINICAL FACTS

This series consists of 15 cases treated by the application of radon seeds sewn to the sclera over the site of the glioma. Twelve were treated at St. Bartholomew's Hospital and 3 at the Moorfields Eye Hospital from 1934-1948 (see Table A). There were 8 males and 7 females. Their ages were between 4 months and 3 years, 6 were under one year old, 6 between 1 and 2 years and 3 between 2 and 3 years of age.

Fourteen were bilateral and one unilateral. The right eye was treated by radon in 7 cases and the left eye in 8. The size of the neoplasm was over  $\frac{1}{2}$  the interior of the globe in 1 case, nearly  $\frac{1}{2}$  in 1, and  $\frac{1}{4}$  in 2. There were 4 separate islands of glioma in 2 cases, 3 in 3 cases and 2 islands in 1 case. There were single masses of growth in 8 cases. The macula was the site of an island of growth in 4 cases.

It is important to search the periphery of the fundus very carefully, for small hemi-spherical masses about 1.5-3 mm. in diameter were seen at the ora serrata in 4 cases. Furthermore it is important to examine the fundus at monthly intervals for a few years to discover islands of glioma arising in parts remote from the original neoplasm treated by radon. Such were found in 3 cases, one 5 months after irradiation, another 4 months later and the third one month after the application of radon seeds to 2 islands of glioma.

The dose of radon and the number of seeds were planned according to the size of the neoplasm. In 2 cases a single application of one 2 millicurie seed was made; in 4 cases 3 seeds were used and in 1 case 4 seeds. Two applications were necessary in 6 cases and 3 applications in 2 cases; and 3 of these were for a new island of glioma arising at a later date and remote from the site of the original growth. In 4 instances the second and third applications of radon were made at the site of the original growth because the destructive effect of the initial application of radon was considered doubtful. Although the changes in the neoplasm made by effective irradiation were evident on ophthalmoscopic examination between the 3rd and 8th day after irradiation and the neoplasm may disappear in 1 to 2 months it is, in some cases of large masses of growth, necessary to wait 5 or 6 months after radon treatment to



be sure that the effect is complete. The site where the seed is sewn to the sclera shows in the fundus a characteristic white and pigmented scar with a crenated edge which appears about the 7th month and is well formed 14 months after irradiation.

If the seed is placed a little remote from the island of glioma, for instance about 3 mm. above or to the temporal side of a neoplasm about 3 mm. in diameter at the macula (as in Case 6), the site of the irradiated growth will appear as a faint greyish discoloration and the position of the radon seed be shown by the characteristic scar described above.

#### COMPLICATIONS

(1) *Cataract*.—In 5 cases irradiation opacities occurred in the lens, in 4 of these the changes were in the centre of the posterior cortex and up to about 1.5 mm. in diameter. In case (11) opacities began 13 months after irradiation and over a period of 6 years extended slightly from the equator of the lens at 2.30 o'clock in direct line with a 2 mc. radon seed which had been sewn to the sclera at the ora serrata.

In the 4 children with central posterior cortical opacities  $4 \times 2$  mc. radon seeds had been placed just behind the equator in one case;  $3 \times 1.1$  mc. seeds at the macula in one case; in another case on 2 occasions at 3 months interval a 1.1 mc. seed had been placed above the optic disc a second 1.1 mc. at the equator and one year and nine months later a 2 mc. seed was placed below the disc; and in the 4th one 2 mc. seed and then  $2 \times 2$  mc. at 6 months interval were placed over the macula and adjacent to the temporal edge of the dural sheath of the optic nerve. In these cases the onset of lens changes after irradiation was 2 years and 2 months, 11 years and 6 months, 4 years and 9 months, and 5 years and 9 months respectively.

In case (1) the lens opacities have gradually spread in the posterior cortex from 1936-1948 and together with peri-macular exudates vision has become reduced to 6/60. Despite this handicap he has completed his education at Manchester Grammar School and passed School Certificate.

(2) *Retinal changes*. (a) *Exudates*.—Greyish irregular-shaped flecks of exudate occurred at and around the macula in 5 cases. In 4 of these relatively heavy doses of radon had been used behind the equator,  $4 \times 2$  mc. seeds in 1 case; in a second case applications consisting of  $2 \times 1.1$  mc. were given on 2 occasions and  $1 \times 2$  mc. on one occasion; applications of  $3 \times 2$  mc. and  $2 \times 2$  mc. in a third case; and in the fourth case one application of  $4 \times 2$  mc. and 7 months later  $2 \times 2$  mc. were used. In the fifth case one 2 mc. was placed above and to the temporal side of a macular growth. In this

last case the distribution of the exudates ultimately resembled those seen in retinitis circinata. The onset of these changes after irradiation was 2 years and 2 months, 1 year and 10 months, 11 months, 7 months and 9 years respectively. The exudates persist for a number of years, up to 11 years has been observed to-date. The occurrence of this complication has been noted in the series only when radon was used behind the equator. It has, however, been seen in a patient suffering from a lesion of haemangiogliomatosis retinae at the ora serrata which Foster Moore treated with radon seeds.

In one of these cases associated with central lens changes vision fell to 6/60, in another from 6/18 to 6/24 and the remaining 2 lost their sight through a severe vitreous haemorrhage in one case and total retinal detachment in the other.

(b) *Haemorrhages*.— Retinal haemorrhages were a late complication in 6 cases. In one instance 2 very small haemorrhages occurred near the equator in the upper nasal quadrant 3 years after irradiation of a neoplasm at the macula and these have persisted at this site for over 8 years. In the other 5 cases the radon seeds had been placed near the main branches of the central retinal vessels within a few millimetres of the optic disc and haemorrhages occurred 6 months, 7 months (2 cases), 11 months, and 1 year after irradiation.

In one patient, Case (3), the haemorrhage was so severe that it extended into the vitreous, causing retinitis proliferans.

(c) *Retinal detachment* occurred in 4 cases. In 2 of these the growth filled about half the eye in case (4) and more than this in case (5). Nearly half the interior of the eye was occupied by 4 islands in case (12) two of which were large. The dark greyish colour of the detachment suggested that between the retina and choroid there existed a mass of cell debris. In none of these cases followed up since 1936 and 1937 has there been any evidence of recurrence of the glioma.

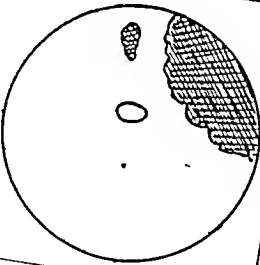
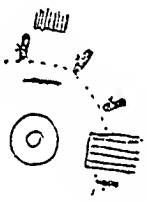
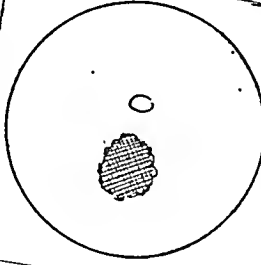

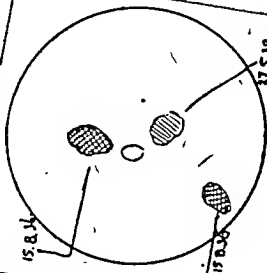
## RESULTS

In all 15 cases the islands of glioma were effectively irradiated by radon seeds.

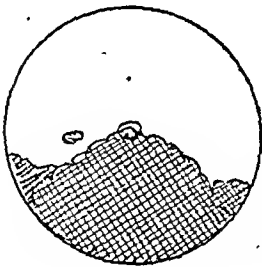

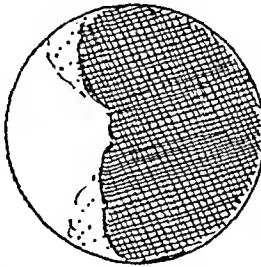
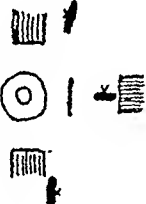
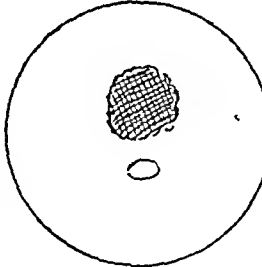

One child, Case (7), died about one year after successful irradiation of a single island of glioma, of which there was no trace on pathological examination after death. The cause of death was not discovered. It was suggested that it might have resulted from the cerebral effects of deep X-ray therapy given to the orbit from which the other eye had been excised.

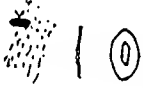
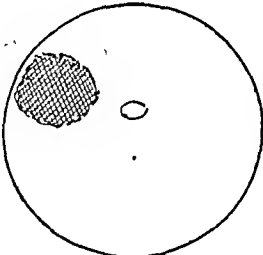
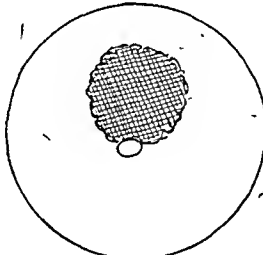


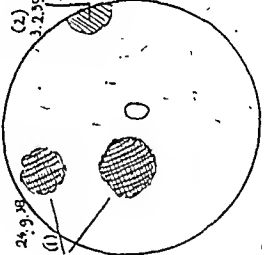


Case (10) was evacuated from St. Bartholomew's Hospital at the outbreak of war, went to Manchester and in January, 1940, on account of complicated glaucoma and the appearance of a suspicious mass near the optic disc the eye was excised.

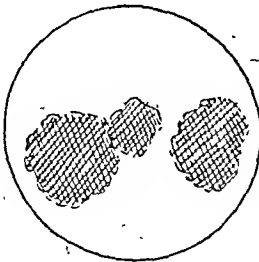




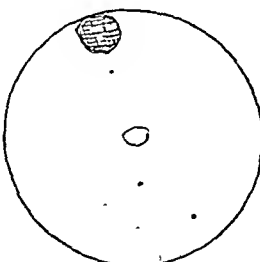




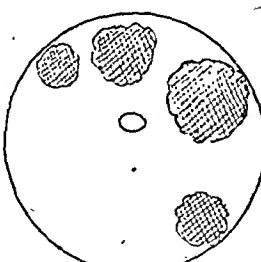


TABLE B

No. Initials and Sex	Age	Date of Radium Treatment	Eye Treated by Radon	Site and Size of Glioma Retinae	Dose in Millieuries	Complications			Results
						Cataract	Retinal Exudates	Other Complications	
(1) J.W. Male	27/12	21.8.34 — 31.8.34	R		4 x 2 mc.  Post equator. 7 mm. apart.	24.10.36 Central post-cortical.	20.9.35 Peri-macular	—	1944. R.V. 6/36. 1946. Passed School Certificate. 1948. R.V. 6/60.
(2) M.B. Male	11/12	26.3.35 — 29.3.35	R		3 x 1.1 mc. 	2.9.46 Central post-cortical slight.	15.4.38 —	15.4.38. One small haem. upper nasal at equator. 2.9.46. Two haemorrhages at same site.	1946. R.V. 4/60. At boarding school.
(3) M.M. Female	4/12	(1) 15.8.36 — 21.8.36 (2) 21.11.36 — 31.11.36 (3) 27.5.38 — 3.6.38	L		Over macula. 2 mm. apart. (1) 2 x 1.1 mc. (2) 2 x 1.1 mc. (3) 2 mc.	8.5.41 Post-cortical opacity slight.	3.6.38 Macular	July 1937. Large haemorrhage above optic disc and macular. April 1939. Recurrence of haemorrhage, same site.	1948. P. L. Schiötz. 32 Hg mm. Shrinking eye.

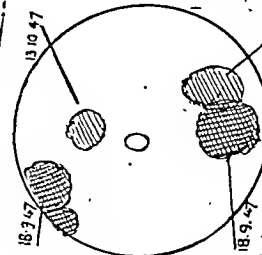


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(4) P.R. Male	8/12	(1) 11.1.37 — 21.1.37 (2) 23.7.37 — 30.7.37	L		(1) 3 x 2 mc. (2) 2 x 2 mc.  Post equator. 7 mm. apart.	—	10 12.37 Macular	21.5.37. Retinal detachment.	1948. Blind College, Worcester. No recurrence. Shrunk eye. Clear cornea and lens.
(5) M.L. Female	15/12	25.10.37 — 2.11.37	R		3 x 2 mc. 	—	—	25.5.38. Total retinal detachment. Retinal haemorrhages ++.	Until 25.5.38 successful irradiation of glioma.
(6) J.K. Female	16/12	27.2.37 — 1.3.37	L		2 mc. 	—	15.3.46 Peri-macular like retinitis circinata.	—	5.6.45. L.V. 6/18. 1.8.46. L.V. 6/24.

No. Initials and Sex	Age	Date of Radium Treatment	Eye Treated by Radon	Site and Size of Glioma Retinae	Dose in Milllicuries  	Complications			Results
						Cataract	Retinal Exudates	Other Complications	
(7) D.E. Male	3	(1) 12.4.38 — 19.4.38 (2) 22.10.38 — 29.10.31	R		(1) 2 mc. (2) 2 x 2 mc.  Between equator and O.D.	—	—	—	Glioma, clinical cure. 1.3.39. Died. Cause unknown. ? Effect of deep X-ray. (for left orbit)
(8) T.M. Male	15/12	(1) 16.7.38 — 23.7.38 (2) 3.1.39 — 14.1.39	L		(1) 2 mc. (2) 2 x 2 mc.   (1) Over macula. (2) Seeds 7 mm. apart up to duaxal sheath.	26.4.44  Post- cortical	—	7.7.39. Retinal haemorrhage adjacent to O.D.	27.4.45. L.V. 6/60. 1948. Reads and writes well. Uses nasal part of retina for fixation.
(9) D.M. Female	7/12	(1) 24.9.38 — 11.10.38 (2) 3.2.39 — 11.2.39	R		(1) 2 mc. between 2 islands.   (2) 2 mc. 	—	—	—	Attends school. Sees her way about.

(10) R.B. Female	1	(1) 14.1.39 — 21.1.39 (2) 29.7.39 — 8.8.39	L	 <p>1 mc. <math>2 \times 2</math> mc.          2 mc. 2 mm. above optic disc.</p>	—	—	18.7.39. Retinal haemorrhage 2 mm. long. Upper temporal edge of central neoplasm.	3.1.40 Left eye excised in Manchester. ? Active growth at O.D. Complicated glaucoma.
(11) J.F. Female	5/12	7.2.39 — 11.2.39	R	 <p>2 mc.    </p>	29.3.40  4.2.46  No further change	—	—	Illiterate. Mentally backward. "Sees well."
(12) J.F. Male	2	(1) 11.8.39 — 19.8.39 (2) 28.3.40 — 4.4.40	R	 <p>(1) <math>4 \times 2</math> mc. Seeds      (2) <math>2 \times 2</math> mc. on stent lower nasal quadrant</p>	—	25.3.40 Macular	25.3.40. Haem. nasal side of O.D. 1948. Shrunken eye. Deep a.c.	1948. Alive and well. 23.11.42. Blind School.

H. B. STALLARD

No. Initials and Sex	Age	Date of Radium Treatment	Eye Treated by Radon	Site and Size of Glioma Retinae	Dose in Millicuries	Complications			Results
						Cataract	Retinal Exudates	Other Complications	
(13) W. B. Male	24/12	13.3.46 — 20.3.46	L		$3 \times 2$ mc. 7 mm. apart. Post-equator.	—	—	—	1948. Sees well.
(14) S. V. Male	11/12	17.7.47 — 24.7.47	L		$3 \times 2$ mc.	—	—	—	12.4.48 Sees well.
(15) J. H. Female	4/12	(1) 18.9.47 — 25.9.47 (2) 23.10.47 — 6.11.47 (3) 22.1.48 — 29.1.48	L		(1) (2)  (3) (4)  2 mc.	—	—	—	15.4.48. Sees well.

Case (5) was the only unilateral case treated by radon seeds in this series. More than half the interior of the eye was occupied by the neoplasm. Excision of the eye had been refused by the parents. It seemed from ophthalmoscopic appearances that the neoplasm had been successfully irradiated. Seven months after this treatment a total retinal detachment and severe retinal haemorrhages occurred.

In Case (4) about half of the interior of the eye was filled with the neoplasm. Five months after irradiation the retina was detached at the site of the neoplasm and ultimately the eye shrank. The cornea and lens have remained clear to-date for 11 years, there has been no recurrence of the neoplasm and the boy has been in good health. He is doing well at the Normal College for the Blind, Worcester.

Case (12) had 4 islands of glioma, 2 of which were large. He had 4 x 2 mc. seeds applied in August, 1939, and one in March, 1940. In November, 1942, the eye became soft, shrunken, the anterior chamber deep, the lens opaque and there was no perception of light. To-date April, 1948, he is alive and well.

Four children (Cases 2, 6, 8 and 9) had neoplasms at the macula. In Case (6) a 2 mc. radon seed was purposely placed away from and above and to the temporal side of the neoplasm at such a distance that the growth was within effective range of the radon seed. As mentioned above the typical scar in the retina and choroid which occurs at the site of the seed did not in this case involve the macula. Except for slight greyish discolouration there was no ophthalmoscopic change at the macula until 9 years after irradiation when some exudate appeared. This child had 6/18 vision which has fallen to 6/24 on account of the exudates. It is interesting to note that vision has been sufficient for school work in the other 3 cases of macular involvement where a radon seed was placed over the macula and the characteristic scar appeared at this site. M.B. (Case 2) saw 4/60 and is doing well at a boarding school. T.M. (Case 8) sees 6/60 with the nasal part of the fundus, writes and draws clearly and reads fluently from a book held about 6 inches from his eye and to the temporal side. J.W. (Case 1), treated in 1934, had good vision until increasing posterior cortical opacities reduced this to 6/60. He has attended Manchester Grammar School and passed school certificate. The lens is to be extracted.

J.F. (Case 11) is illiterate and mentally backward, she attends school and it is evident that she sees reasonably well playing games. Of the remaining 4 children 3 are at present too young for accurate visual acuity tests, but it is clear that they see objects about them and when they have become old enough have been able to dress, feed themselves and join in games with other children.

To sum up. In this series there has been one death (cause unknown) whose eye was successfully irradiated. Four have become blind, in 3 of these the irradiated eyes shrank, one after a severe vitreous haemorrhage and retinitis proliferans and the other 2 after retinal detachment, and the fourth had her eye excised in Manchester because of a suspected recurrence. In one case the disease was unilateral, a retinal detachment and retinal haemorrhages destroyed the sight of the irradiated eye. The remaining 9 (60 per cent.) children have attended schools and have enjoyed sufficient sight for educational needs, to see their way about and to participate in most games.

#### COMMENTARY

The treatment of glioma retinae by radium is under trial, with changes in technique, and the dose is at present empirical. It seems that a dose of 3,500 r is effective in destroying this very radiosensitive neoplasm. The method of interstitial irradiation



by the insertion of a radon seed through the sclera into the substance of the neoplasm has been abandoned for that of suturing the seed, or several seeds at appropriate intervals of 7 mm. to the sclera over the site of the glioma marked out on the sclera by surface diathermy and checked by ophthalmoscopic examination. Trial is now being made with radium plaques of silver or aluminium 0.5 mm. thick containing radium salt, shaped to the radius of curvature of the sclera and secured thereto with fine silk sutures.

The results of treatment are good when the neoplasm occupies a quadrant or less of the globe and the visual result is better when the islands of glioma are at or in front of the equator. In the case of a growth at or near the macula and optic disc it is preferable, in order to avoid the dense choroido-retinal scarring which occurs immediately beneath the site where the radium is placed on the sclera and damage to the larger branches of the central retinal vessels, to place the source of radium a little remote from the growth, towards the periphery but leaving it within the range of effective irradiation.

Serious complications such as retinal detachment, large intra-ocular haemorrhages and ultimately shrinkage of the globe occur in cases where about half or more of the interior of the eye is occupied by the neoplasm and when it has been necessary to place radon seeds over the large branches of the central retinal vessels as these curve near the optic disc.

In my opinion it will be justifiable in future to treat unilateral cases of glioma by radium if the neoplasm occupies a quadrant of the globe or less. However, it is seldom that an infant is brought for examination at such a stage and generally half or more of the retina is destroyed before attention is drawn to the disease.

#### MALIGNANT MELANOMA OF THE UVEAL TRACT

Stanford Cade writes "Malignant melanomata are radio-resistant tumours and their treatment by radiation is both difficult and disappointing. It is, however, unfortunate that radioresistance—a comparative term used to indicate the degree of sensitivity to radiation of one tissue as compared with another—should have been given a meaning synonymous with that of 'unsuitability for radiation' " and Ellis comments "this attitude (that melanomata are radioresistant and unsuitable for radiotherapy) moreover seems to be so universally adopted at radiotherapeutic centres in various parts of this country and America, that it would seem the time is ripe for suggesting the contrary opinion, for which there can be adduced a good deal of evidence of an incontrovertible kind, that some melanomas, at any rate, are radiosensitive."

H. Barkan commented in 1934 that the literature contained no case of malignant melanoma cured by radium. Transient regression of the neoplasm has been noted by Parker, Stokes, Janeway and Birch-Hirschfeld. Microscopic examination of excised eyes showed extensive regression but there remained small areas of well-stained and active tumour cells.

To date, the material for radiotherapy has been too small to assess the relative radiosensitivity of the various types of cell found in malignant melanomata—*e.g.*, spindle-cell (a) and (b), fascicular, endothelial, and mixed-celled neoplasms. It is evident that better results are obtained when the growth is lens-shaped, has not ruptured Bruch's membrane, and is in the vicinity of the equator. The results are appreciably less fortunate when the neoplasm involves the ciliary body and when it is adjacent to the optic disc.

Radiotherapy is justifiable in rare cases of bilateral malignant melanoma of the choroid and I think in the future this may be so for some cases of unilateral growths seen in the early stages. The following case report is an instance of a bilateral malignant melanoma of the choroid in which the neoplasm in the second eye has remained inactive 9 years after irradiation.

E.H., aged 36 (in 1939), had his left eye excised for malignant melanoma of the choroid in April, 1939. Microscopic examination showed a pigmented spindle-celled neoplasm. In the right eye a lens-shaped greyish-brown swelling was seen on the nasal side about the equator between the 2.30 o'clock and 4 o'clock meridians. Its size was assessed as carefully as possible by ophthalmoscopic examination and at operation its limits were marked out by four surface diathermy applications to the overlying sclera and checked by the ophthalmoscope. Within this marked quadrilateral area whose sides measured 8, 5, 8 and 3 mm. respectively 3 x 2 mc. radon seeds were sewn to the sclera. The depth of the growth had been approximately assessed by the ophthalmoscope at 4 mm.

In eight weeks the neoplasm was reduced to a flat plaque and it has remained thus with no sign of activity to-date April, 1948. The vision of this eye is 6/5. There are a few vacuoles in the upper nasal quadrant of the posterior cortex of the lens but these cause no visual disturbance.

Another case of a malignant melanoma adjacent to the optic disc on the nasal side was successfully irradiated in 1940, has kept his eye to-date (1948) but some obliteration of small vessels in the optic disc caused optic atrophy to become evident 7 to 8 weeks after irradiation.

Three other cases of malignant melanoma of the choroid and one of the ciliary body have been treated by radon seeds at St. Bartholomew's Hospital. In one case in 1932 there was a mushroom-shaped malignant melanoma of the choroid which had burst through Bruch's membrane just behind the equator. The neoplasm diminished in size after irradiation with 4 radon seeds and 5 months after operation it seemed likely on ophthalmoscopic examination that some viable neoplasm was still present and so

the eye was excised. After excision the neoplasm measured 9.9 x 7 x 4 mm. The area of effective irradiation as judged by microscopic evidence of chromatolysis, necrobiosis, degenerative changes and obliteration of the blood vessels was found in serial sections to be 8.5 x 6 x 2 mm.

Another case of malignant melanoma of the choroid in an only eye was treated by 4 x 1 mc. radon seeds on October 8, 1935, the growth shrank to a flat plaque and remained so till December, 1937, when it began to grow again. The lower half of the retina became detached and the vision reduced to hand movements. It seemed justifiable to attempt local excision after reflecting a scleral flap. This was done by a combination of surface diathermy along the lines planned for the scleral flap incision and a cutting diathermy needle in the choroid around the base of the neoplasm when this was exposed. The neoplasm was removed without loss of vitreous and with no apparent damage to the retina which was seen in the wound after removal of the growth and before tying the sutures in the scleral trap-door. This was done on December 17, 1937. The post-operative course was remarkably uneventful till a vitreous haemorrhage occurred during the third week. The patient was alive and well when he was last heard of in September, 1939. He could see his way about in familiar surroundings, but could not read. He declined to attend hospital for further follow-up examinations.

In another case of malignant melanoma of the choroid the growth was markedly reduced in size, the patient died about 1½ years later of some other disease. He was a Jew and his relatives refused post-mortem examination, so a valuable specimen was lost.

One case of richly pigmented malignant melanoma of the ciliary body between 2 and 5 o'clock was treated by 3 x 2 mc. radon seeds sutured to the sclera. The neoplasm shrank in 8 weeks to half its size. Fourteen weeks after operation pain, lacrimation, conjunctival congestion and photophobia made the patient request excision of the eye.

#### METASTATIC CARCINOMA OF THE CHOROID

If this occurs in an only eye or, as it rarely does, in both eyes, irradiation by radon seeds is successful and justifiable in so far that this procedure saves the eye and some measure of sight which the sufferer is able to enjoy before he dies.

I thank the following surgeons for recommending patients: Mr. Gibb, Mr. Neame, Mr. Doyne, Mr. Davenport and Mr. Rycroft (London); Mr. Stirling and Mr. MacNabb (Manchester); Mr. Holmes (Liverpool); Mr. Ashdown Carr (Derby); Mr. Gann (Peterborough); Mr. Aitchison (Newcastle-upon-Tyne); Mr. Galloway (Nottingham); and Mr. Colley (Bath).

I also thank Mr. Stewart and Mr. G. S. Innes, Radium Department, St. Bartholomew's Hospital, for valued advice.

In conclusion I express my lasting gratitude to my late chiefs. To Mr. Foster Moore for the privilege I enjoyed of assisting him in his pioneer work on this subject, for the stimulus of his clear and honest observations, and for his generosity in allowing me to treat some of his cases at St. Bartholomew's Hospital. To Sir John Parsons, that "Master" of the physiology and pathology of the eye, I owe a high example of the manner in which to seek academic truth.

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## A POINT FOR CONSIDERATION IN THE USE OF THE STEREOSCOPE

BY

FRANK W. LAW

LONDON

It recently occurred to the writer that it would be of value to know the answer to the question "What happens to the inclination of the visual axes on moving the stereogram in a stereoscope towards or away from the observer?" The question seemed simple; the answer was not obvious. Further, enquiry in various directions discovered the somewhat consoling result that the answer was not generally known; indeed, it had not been considered by most of those asked, which is surprising, in view of the common habit of sending a patient home to "do exercises with a stereoscope."

On investigating the subject it is soon apparent that the interocular distance is a factor of fundamental importance. This can be demonstrated by considering three diagrams (Figs. 1, 2 and 3) in which the stereogram card is depicted as placed at three different distances from the lenses of the instrument. Fig. 1 shows it placed at the focal plane; the emergent pencil of light has parallel rays, and the amount of convergence is independent of the interocular distance. In Fig. 2 the card is represented as nearer than the focal plane; the emergent pencils are divergent and greater inter-

ocular distance involves greater convergence. In Fig. 3, with the card beyond the focal plane, the emergent pencils are convergent, and greater interocular distance involves less convergence. In each figure the lens combinations are represented diagrammatically; the optical centres are at 0.

One may now re-consider the phenomenon depicted in the figures by studying a chart obtained by calculation. Table I shows the

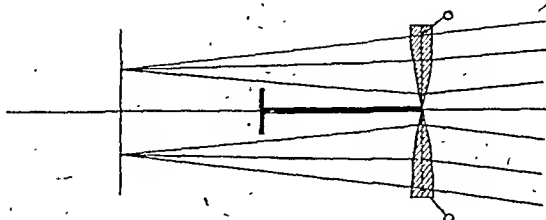


FIG. 1.

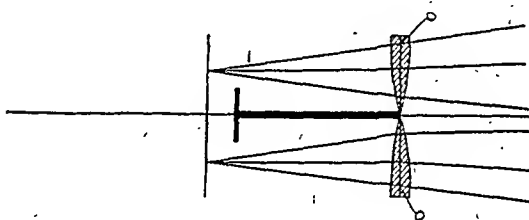


FIG. 2.

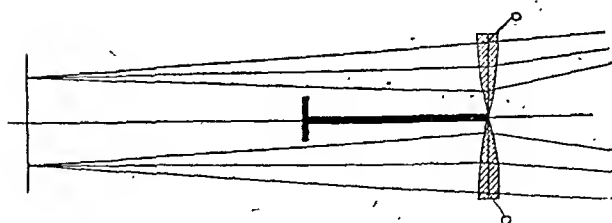


FIG. 3.

calculations for a stereoscope with lenses of  $+5.0D.$ , optical centres  $8.8$  cms. apart, pictures separated by  $5$  cms. Three positions of the stereogram are considered. The fact, depicted in Fig 1, that when the card is placed at the focal plane, convergence is independent of interocular distance, emerges at once. Other interesting facts also appear; the same stereogram moved in the same direction and through the same distance induces an increase of convergence when the interocular distance is  $5.2$  cms., a smaller increase when it is  $5.4$  cms., and an actual decrease when

it is 5.8 cms. Further, with the card at 25 cms., a greater interocular distance involves a reduced degree of convergence.

Table II, calculated for a stereoscope with lenses of +4.0D., optical centres 9 cms. apart, and 5 cms. separation of the stereograms, shows lower convergence figures, but exactly the same tendencies.

TABLE I

Width of Stereo-gram	Distance from Lenses	Interocular Distance			
		5.2 cm.	5.4 cm.	5.8 cm.	6.2 cm.
		Conver	gence in	Prism	Dioptres
5 cm.	10	17.2	18.1	19.8	21.6
	20	19.0	19.0	19.0	19.0
	25	19.4	19.2	18.7	18.3

TABLE II

Width of Stereo-gram	Distance from Lenses	Interocular Distance			
		5.2 cm.	5.4 cm.	5.8 cm.	6.2 cm.
		Conver	gence in	Prism	Dioptres
5 cm.	11 cm.	14.7	15.5	16.3	17.1
	25	16.0	16.0	16.0	16.0
	33.3	16.3	16.1	15.7	15.3

The practical deduction to be made from the above is that, once one has decided for what exact purpose one requires a patient to use a stereoscope, it is essential to choose an appropriate instrument and, having measured the patient's interocular distance, to calculate how the instrument will have to be used, and instruct the patient accordingly. With this in view, tables have been constructed showing the actual deviation of the visual axes involved for varying width of stereogram, and varying positions of the pictures. In Table III the basis is for lenses of 5.0D., optical centres 8.8 cms. apart; in Table IV the lenses are 4.0D. in strength, with optical centres 9 cms. apart. In each case the distance from lens to ocular centre is assumed to be 3 cms.; + (plus) indicates convergence and - (minus) divergence.

The heavy stepped line which crosses each Table is an important line of demarcation. It will be seen that the figures above this line demonstrate a common tendency—that an approach of the stereograms towards the eyes causes an increase of convergence; those below the line, that an approach of the stereograms towards

the eyes causes a decrease in convergence, or an increase in divergence.

The practical application of these Tables would be relatively simple. Having ascertained the patient's interocular distance one can see at a glance which card and which direction of movement will give the effect desired in the particular case to be treated. This will at least prevent the patient from being asked to do exercises inappropriate to his condition—and one cannot but feel that such an event must have occurred. It may, however, be considered that, when convergence or divergence is the only factor which it is desired to vary, a simpler course would be to give the patient a stereoscope with rotating prisms and place the stereograms in the focal plane.

TABLE III

Stereogram		Interocular Distance (cm.)							
Width	Distance from Lens	4'6	4'8	5'0	5'2	5'4	5'8	6'2	6'6
3 cm.	10 cm.	+ 32'2	33'1	34	34'9	35 8	37'6	39'4	41'2
	20	+ 29	29	29	29	29	29	29	29
	25	+ 28'3	28'1	27'9	27'7	27 5	27'1	26'7	26'3
4 cm.	10 cm.	+ 23'4	24'3	25'2	26'1	27	28'8	30'6	32'4
	20	+ 24	24	24	24	24	24	24	24
	25	+ 24'1	23'9	23'7	23'5	23'3	22'9	22'5	22'1
5 cm.	10 cm.	+ 14'6	15'5	16'4	17'2	18'1	19'8	21'6	23'4
	20	+ 19	19	19	19	19	19	19	19
	25	+ 20	19'8	19'6	19'4	19'2	18'7	18'3	17'9
6 cm.	10 cm.	+ 5'8	6'7	7 6	8'4	9'3	11	12'8	14'6
	20	+ 14	14	14	14	14	14	14	14
	25	+ 15'9	15'7	15'5	15'3	15'0	14 6	14'2	13'8
7 cm.	10 cm.	— 2'9	— 2	— 1'1	— 0'2	+ 0'6	+ 2'3	+ 4'1	+ 5'8
	20	+ 9	+ 9	+ 9	+ 9	+ 9	+ 9	+ 9	+ 9
	25	+ 11'8	+ 11'6	+ 11'4	+ 11'2	+ 11	+ 10'5	+ 10'1	+ 9 7
8 cm.	10 cm.	— 11'4	— 10'5	— 9'6	— 8'7	— 7'9	— 6'2	— 4'4	— 2'7
	20	+ 4	+ 4	+ 4	+ 4	+ 4	+ 4	+ 4	+ 4
	25	+ 7'6	+ 7'4	+ 7'2	+ 7	+ 6'8	+ 6'4	+ 6	+ 5'6
9 cm.	10 cm.	— 20'1	— 19'2	— 18'3	— 17'4	— 16'6	— 14'9	— 13'1	— 11'3
	20	— 1	— 1	— 1	— 1	— 1	— 1	— 1	— 1
	25	+ 3'5	+ 3'3	+ 3'1	+ 2'9	+ 2'7	+ 2'3	+ 1'9	+ 1'5
10 cm.	10 cm.	— 28'8	— 27'9	— 27	— 26'1	— 25'3	— 23'5	— 21'7	— 19'9
	20	— 6	— 6	— 6	— 6	— 6	— 6	— 6	— 6
	25	— 0'6	— 0'8	— 1	— 1'2	— 1'4	— 1'8	— 2'2	— 2'6
11 cm.	10 cm.	— 37'6	— 36'7	— 35'8	— 34'9	— 34'1	— 32'3	— 30'5	— 28'7
	20	— 11	— 11	— 11	— 11	— 11	— 11	— 11	— 11
	25	— 4'8	— 5	— 5'2	— 5'4	— 5'6	— 6	— 6'4	— 6'9

TABLE IV

Stereogram		Interocular Distance (cm.)							
Width	Distance from Lens	4'6	4'8	5'0	5'2	5'4	5'8	6'2	6'6
3 cm.	11 cm.	+ 27'6	28'5	29'4	30'3	31'1	32'9	34'7	36'4
	25	+ 24	24	24	24	24	24	24	24
	33'3	+ 23'1	22'9	22'7	22'5	22'3	21'9	21'5	21'1
4 cm.	11 cm.	+ 19'8	20'7	21'6	22'5	23'3	25'1	26'9	28'6
	25	+ 20	20	20	20	20	20	20	20
	33'3	+ 20	19'8	19'6	19'4	19'2	18'8	18'4	18
5 cm.	11 cm.	+ 12	12'9	13'8	14'7	15'5	16'3	17'1	20'8
	25	+ 16	16	16	16	16	16	16	16
	33'3	+ 16'9	16'7	16'5	16'3	16'1	15'7	15'3	14'9
6 cm.	11 cm.	+ 4'2	5'1	5'9	6'8	7'7	9'4	11'2	13
	25	+ 12	12	12	12	12	12	12	12
	33'3	+ 13'8	13'6	13'4	13'2	13	12'6	12'2	11'8
7 cm.	11 cm.	— 3'6	— 2'7	— 1'9	— 1	— 0'1	+ 1'6	+ 3'4	+ 5'2
	25	+ 8	+ 8	+ 8	+ 8	+ 8	+ 8	+ 8	+ 8
	33'3	+ 10'7	+ 10'5	+ 10'3	+ 10'1	+ 9'9	+ 9'5	+ 9'1	+ 8'7
8 cm.	11 cm.	— 11'4	— 10'5	— 9'6	— 8'8	— 7'9	— 6'2	— 4'4	— 2'6
	25	+ 4	+ 4	+ 8	+ 4	+ 4	+ 4	+ 4	+ 4
	33'3	+ 7'6	+ 7'4	+ 7'2	+ 7	+ 6'8	+ 6'4	+ 6	+ 5'6
9 cm.	11 cm.	— 19'2	— 18'3	— 17'4	— 16'6	— 15'7	— 14	— 12'2	— 10'4
	25	0	0	0	0	0	0	0	0
	33'3	+ 4'5	+ 4'3	+ 4'1	+ 3'9	+ 3'7	+ 3'3	+ 2'9	+ 2'5
10 cm.	11 cm.	— 27	— 26'1	— 25'2	— 24'4	— 23'5	— 21'8	— 20	— 18'3
	25	— 4	— 4	— 4	— 4	— 4	— 4	— 4	— 4
	33'3	+ 1'4	+ 1'2	+ 1	+ 0'8	+ 0'6	+ 0'2	— 0'2	— 0'6
11 cm.	11 cm.	— 34'8	— 33'9	33	32'3	31'3	29'6	27'8	26'1
	25	— 8	8	8	8	8	8	8	8
	33'3	— 1'7	1'9	2'1	2'3	2'5	2'6	3'3	3'7

If, however, accommodation is also to be varied, the simpler stereoscope is more effective—again provided that one is fully aware of how it should be used; and this brings one to the interesting consideration of the relationship, when using a stereoscope, between accommodation and convergence. In this connection a Table has been calculated showing the position of any card at which accommodation balances convergence. The range over which this can obtain is limited. Cards separated by a distance of less than 4 cms. cannot be brought sufficiently close to the lenses to induce the required amount of accommodation. On the other hand, beyond the focal plane accommodation is absent



or negative, and cards separated by more than 10 cms. require divergence in all positions for superimposition to occur. Within the remaining range, however, the convergence can be calculated from the figures in Tables III and IV and expressed in metre-angles by dividing the figure representing prism. dioptres of convergence by the interocular distance in cms. Thus, taking the first item in Table III,  $\frac{32.2}{4.6} = 7$  M.A. The results are shown in Table V, and are of interest in demonstrating the wide fluctuations in the accommodation factor induced by movement of the stereograms. The Table enables one to apply an exercise for

TABLE V

Stereogram Width	5 OD. LENSES		4 OD. LENSES	
	Distance from Lens	Acc (D) = Conv (M.A.)	Distance from Lens	Acc (D) = Conv (M.A.)
4 cms.	9.5	4.5	11.7	4.4
5 cms.	11.4	3.4	15	2.9
6 cms.	13.8	2.2	18	1.9
7 cms.	16.4	1.2	20.2	1.1
8 cms.	18.5	0.5	22.8	0.5
9 cms.	20	0	25	0

improving accommodation and convergence together with scientific accuracy; the bar of the stereoscope could with advantage be marked to indicate the accommodative effort demanded.

It is a pleasure to express my grateful thanks for the courteous and enthusiastic collaboration of Mr. S. P. Holloway in the preparation of this article, and for his drawing up of the Tables.

# THE EFFECT OF AGE AND ILLUMINATION UPON VISUAL PERFORMANCE WITH CLOSE SIGHTS

BY

H. C. WESTON

## 1. INTRODUCTION

THIS paper is based upon the results of an experimental investigation, in which twelve subjects performed a series of special visual tasks involving the perception of fairly small detail. Each task in the series was performed at each of six values of illumination which were so chosen as to form a geometric series. The lowest value was 0.5 lumen per square foot (*i.e.*, 0.5 foot-candle), and the highest was approximately 500 lm/ft<sup>2</sup>, so that the range covered all values likely to be used in practice for comparable tasks done either with natural or artificial lighting. The brightness of the visible environment (panoramic brightness) was varied *pari passu* with that of the local field of attention, so as to maintain a ratio of the former to the latter of not less than 0.5.

As it was not the object of the experiments to obtain data relating to the variation of visual performance with age, the subjects were not chosen accordingly. Subsequently, however, it was found that they were distributed by age in five consecutive quinquenniads covering, approximately, the middle third of life. Hence, the data obtained relate to five small groups, in three of which there were two subjects, while in each of the other two groups there were three subjects. An unusual and, for the present purpose, a very fortunate circumstance, is that similar visual performance tests were done under similar illuminations by the same subjects at times separated by an interval of five years. So, it is possible not only to compare the performances of the five different age groups, but also to show the effect of a five year difference of age upon the performance of each group.

## 2. REFRACTION AND ACUITY OF SUBJECTS

All the subjects are experienced observers, being members of the scientific staff of the National Physical Laboratory. Prior to the second series of experiments, they were examined by Mr. Graeme Talbot, F.R.C.S., and new glasses were prescribed as required (see Table I).

All the subjects read J.I. with their glasses. One is a fairly high myope, but the others are only slightly ametropic. Group

acuity does not appear to be related to group age and, in fact, the clinical findings show no important difference of acuity among the group.

Age Group at Date of refraction	Subject	R. eye	L. eye	Phoria at near
24-28	1	$\frac{-0.25}{-0.25 \cdot 175^\circ} = 6/5$	$\frac{-0.25}{-0.50 \cdot 170^\circ} = 6/5$	0
	2	$\frac{-2.5}{-0.5 \cdot 50^\circ} = 6/6$	$\frac{-2.5}{-0.5 \cdot 30^\circ} = 6/6$	<sup>4</sup> ESO
29-33	3	$\frac{-0.5}{+0.50 \cdot 95^\circ} = 6/6$	$\frac{-0.5}{+0.75 \cdot 60^\circ} = 6/12$	<sup>3</sup> ESO
	4	$\frac{0}{+0.25 \cdot 95^\circ} = 6/6$	$\frac{0}{+0.25 \cdot 80^\circ} = 6/6$	0
	5	$\frac{0}{-2.50 \cdot 10^\circ}$	$\frac{-0.25}{-1.75 \cdot 173^\circ}$	0
34-38	6	$\frac{-1.25}{-0.50 \cdot 160^\circ} = 6/5$	$\frac{-1.0}{-0.5 \cdot 55^\circ} = 6/5$	<sup>4</sup> ESO
	7	$\frac{+3.0}{+0.75 \cdot 83^\circ} = 6/5$	$\frac{+0.25}{-} = 6/5$	<sup>2</sup> EXO
39-43	8	$\frac{-0.25}{+1.0 \cdot 105^\circ} = 6/5$ NEAR ADD.	$\frac{-}{+0.5 \cdot 90^\circ} = 6/5$ $+0.5$	<sup>4</sup> EXO
	9	$\frac{-}{+0.5 \cdot 10^\circ} = 6/6$ NEAR ADD.	$\frac{-0.25}{+0.5 \cdot 145^\circ} = 6/6$ $+0.25$	0
	10	$\frac{-1.0}{-0.5 \cdot 70^\circ} = 6/6$	$\frac{-1.25}{-0.25 \cdot 35^\circ} = 6/6$	0
44-48	11	$\frac{-0.25}{+0.5 \cdot 25^\circ} = 6/5$ NEAR ADD.	$\frac{-0.25}{+0.50 \cdot 110^\circ} = 6/6$ $+1.25$	<sup>4</sup> EXO
	12	$\frac{-9.5}{-1.0 \cdot 105^\circ} = 6/6$ NEAR ADD.	$\frac{-12.5}{-0.5 \cdot 10^\circ} = 6/9$ $+2.0$	<sup>16</sup> EXO

## 3. MEASUREMENT OF VISUAL PERFORMANCE

In this paper *visual performance* means the *rate* of accomplishing a specific visual task, *e.g.*, the discrimination of visual objects having a prescribed characteristic, when these objects are presented along with others in an objective field of sight whose angular size is typical of "near work." The test-objects employed were Landolt rings, arranged as shown in Fig. 1. The rings differ only in the orientation of the gap, eight positions of the latter being used. The visual task consisted in finding all the rings

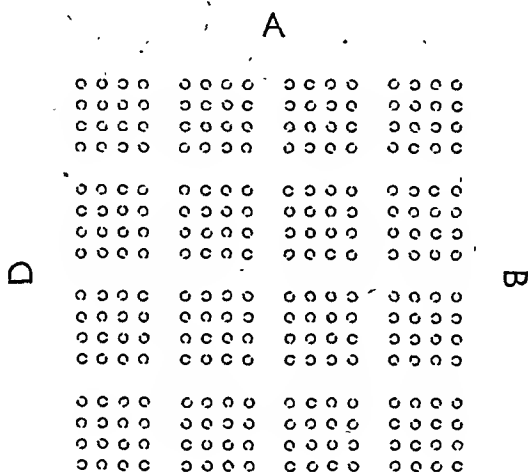


FIG. 1

having the gap in one prescribed position, and so it involved some scrutiny of every ring present in "the sight." The severity of the visual task was varied by using three sizes of ring, such that, at ordinary reading distance, the visual angles subtended by the gaps were, respectively, 1.5, 3 and 4.5 minutes of arc. Of these sizes, the intermediate one corresponds approximately to the size of detail in the news columns of the daily press.

These visual tasks may be compared with practical tasks such as proof-reading, reading numerals, and many inspection tasks done in factories, offices, schools, etc. Clearly the rate of performance can only be ascertained by measuring the time taken by viewer to complete the task. But, as some reaction is necessary for the purpose of indicating that the objects of search have been recognized, the total time taken to deal with each test sight must include this reaction or motor response time. The two components of the time per test, that is, the visual discrimination time and the

indicator action time, cannot be separately measured; hence, an exact determination of the discrimination time is impossible, though, by a suitable technique, it can be ascertained to a fairly close approximation. In these tests the method adopted was as follows. The subjects were asked to indicate the prescribed rings by cancelling them with a stroke of the pencil. They were first given a test sheet on which all the prescribed rings were made extremely conspicuous by being filled in with red ink, thus converting them to red spots. By this means the search time was minimised, the time taken by the subject to work through the test material being almost entirely time occupied in manual action. The test was then given in the ordinary way, so that the prescribed objects had to be found by discerning the gaps in the rings and their orientation. The time required to work through the test material in this way was measured, so that the time per correct ring cancelled could be found. From this was deducted the time required for the act of cancellation, as found from the red-spot test. The net time thus obtained is the closest practicable approximation to the actual discrimination time. This has been corrected when necessary, so as to allow for the fact that the subjects sometimes overlooked some of the rings which should have been cancelled, that is to say, it has been divided by an accuracy factor so as to obtain the time which would have been required for a perfectly accurate performance. The reciprocal of this corrected value is the index of speed of discrimination used in this paper.

#### 4. RESULTS OBTAINED

The individual performance values obtained at each illumination, and with each visual task, have been averaged for each age group. From these averages graphs were prepared showing the variation of performance with illumination. As would be expected, owing to the small number of observations available for each age group at any one illumination and size of test-object, all the points plotted did not lie upon smooth curves. Allowing, however, for unmistakably exceptional results, smooth curves were fitted to the plots, and the performance values derived from these curves are those which have been used in preparing Figs. 2, 3, and 4. In this connection it should be said that the smoothing of the actual observations, while it removes irregularities which are unlikely to have appeared had more data been available for analysis, does not effect the main conclusions to be drawn from these experiments; that is to say, the invariable decline of visual performance with age which is exhibited by the diagrams is found also, and on the average to the same extent, by comparison of the raw data.

Referring now to Fig 2, it can be seen that the points plotted

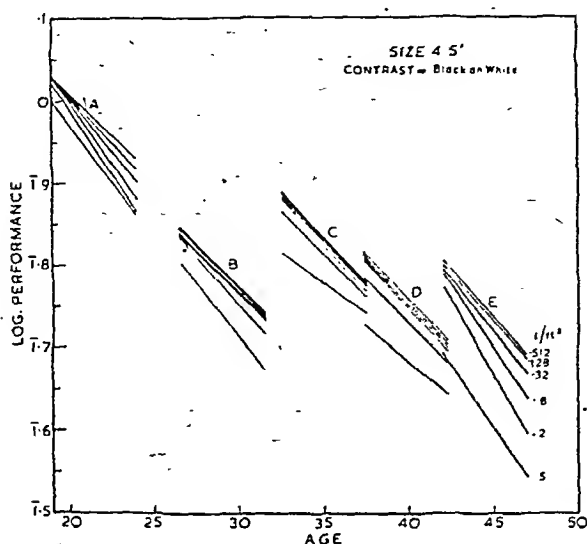


FIG. 2.

refer to ages ranging from 19 to 47 years; and to the logarithms of the value of visual performance. By plotting log. performance all the results are shown on a relative basis, that is to say, the difference on the vertical scale between any two values, is proportional to the *ratio* of those values, and this ratio can readily be found, if desired, from tables of antilogarithms. For example, the scalar difference between the value plotted for group E at 32 lm/ft<sup>2</sup> and age 47 years, and that plotted for group A at the same illumination and age 24 years is 0.23, which means that E's performance is only equal to 59 per cent. of A's. Similarly, it can be found that A's performance at 0.5 lm/ft<sup>2</sup> and age 24, is about equal to 85 per cent. of the performance achieved by the same group at the same age when the illumination was increased to 500 lm/ft<sup>2</sup>.

In Fig. 2 all the lines joining pairs of points have a downward slope, so that it is clear that an advance in age of 5 years is accompanied by a decline in performance in the case of each group, and with all the values of illumination. Consistent with this finding is the obvious decline from group to group as the group-age advances. The general trend of the results might be shown by drawing a straight line across the diagram in such a way that approximately an equal number of all the points plotted lies above and below the line. If this were done it would be found that the downward slope of this line is less steep than that of the lines drawn for each separate age group, so that the annual rate of decline which might be estimated in this way would be lower than

the rate found from the 5-year difference of performance actually observed for each group. One reason for this apparent discrepancy is that the relative levels of the group families of curves certainly depend partly upon group differences of visual ability which, no doubt, existed when all the subjects of these experiments were of the same age. As to this, it is clear that no direct evidence can be had, but the disposition of the families of curves, and particularly the obvious displacement of the B group family, leaves little room for doubt that the different groups would have been found unequal in efficiency could their performance have been measured when they were of equal age. Thus, the decline in performance from one age group to next does not indicate the true rate of decline with advancing age. The true rate can only be found from chronologically different performances of the same individuals or groups, such as are here presented. But, since these chronologically different performances refer only to a 5-year change of age, they do not enable the annual rate of decline to be found for the whole middle third of life, nor do they show whether the rate is constant or variable during this period. On these points, however, the results shown in Fig. 2 are suggestive. It can be seen that, except at the lower values of illumination, the slope of the curves is much the same for each age group, and so, for the particular visual task considered, it would appear that the rate of decline does not vary much from year to year, though it tends to increase during the last quinquennium, *i.e.*, between the ages of 42 and 47. On the average, it is of the order of 5 per cent. per annum with moderate to high values of illumination.

The illumination relating to each performance curve is shown in Fig. 2. It is evident that varying the illumination of the test material has a more marked effect upon visual performance as age advances and, in the case of group E, the spread of the family of curves is twice as wide as it is for group A. It may be noted that, at the age of 45, the performance achieved with an illumination of 500 lm/ft<sup>2</sup> is not as good as that achieved at the age of 25 years, with an illumination of only 0.5 lm/ft<sup>2</sup>. Moreover, after the lapse of 5 years, no group gives the same performance at the highest illumination as it formerly did at the lowest illumination. Although this result is surprising, and is not consistent with the results obtained with smaller test-objects, it seems clear that any considerable advance in age cannot be fully compensated by any reasonable adjustment of the illumination level for visual tasks of this kind.

Turning now to Fig. 3, it will be seen that the decline from group to group is somewhat steeper than it is with the larger test-object dealt with in Fig. 2. But the annual rate of decline, as indicated by the different families of curves, is much the same. Here, however, in the case of the older subjects—groups C, D,

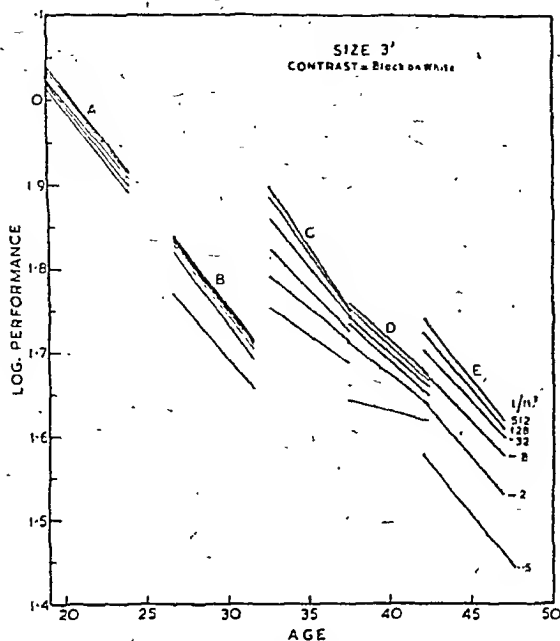


FIG. 3.

and E—an illumination of  $8 \text{ lm/ft}^2$  gives a performance similar to that achieved 5 years earlier by the same subjects with an illumination of  $0.5 \text{ lm/ft}^2$ ; while  $500 \text{ lm/ft}^2$  gives a performance similar to that formerly given by  $2 \text{ lm/ft}^2$ , though, again, it is evident that high illumination does not fully compensate for any considerable advance in age.

Fig. 4 shows the results obtained for the most difficult visual task. As might be expected, the greatest decline from group to group is here exhibited, and the average annual rate of decline throughout the age span considered is more than 7 per cent. The spread of the families of curves relating to age groups B, C, D, and E is much wider than is the case with the easier visual tasks, thus showing that the performance of all the subjects in these age groups, *i.e.*, those whose age is 25 years or more, is much affected by the level of illumination, particularly when this falls below about  $30 \text{ lm/ft}^2$ . Actually, a change from the lowest to the highest illumination tried increases the performance of the youngest subjects only by 18 per cent., but it increases the performance of the oldest subjects fourfold. It is also of interest to note that, with the lowest illumination and the finest visual task, the performance of subjects aged 24 years is just as good as that of subjects aged 47 years with the easiest visual task, and the highest illumination (compare Figs. 2 and 4).



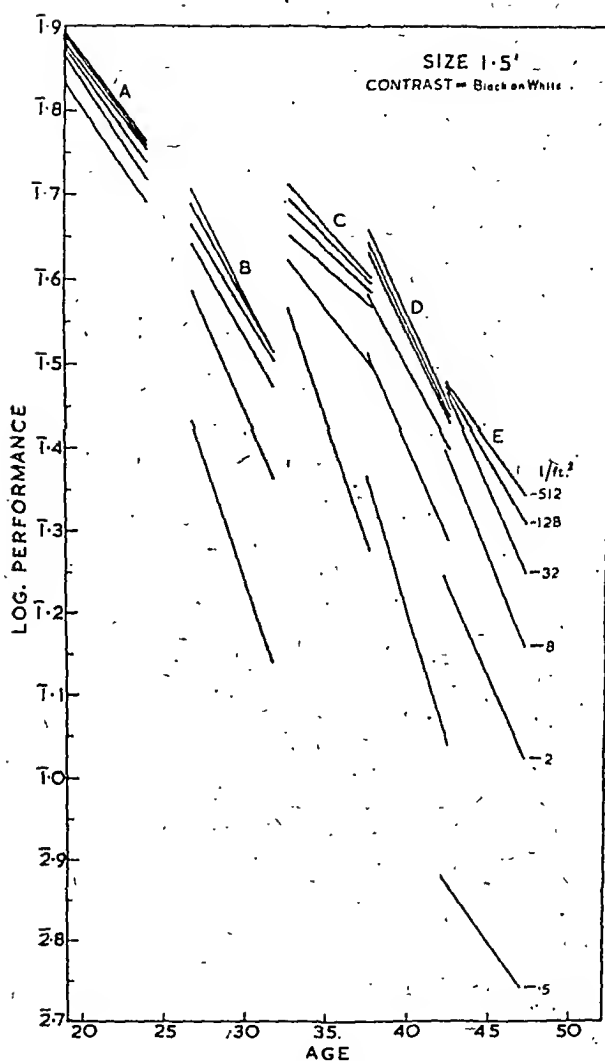


FIG. 4.

### 5. CONCLUSION

It should be clearly understood that the decline shown by the results of the experiments discussed does not refer to the resolving power of the eyes, but to the quickness of perception, that is, to a function of vision which is not evaluated by clinical tests. Even so, the extent of the decline, and its early onset, may seem surprising, and perhaps depressing. It must be remembered, however, that most everyday visual tasks do not involve continuous scrutiny of small detail, and so the performance of them will not generally be so much affected in the advance to "middle-age"

as is the performance of the visual tasks considered in this paper. Nevertheless, visual efficiency appears to come to its maximum in early adulthood, and, thereafter, to fall off at a greater rate than we realise. This is in keeping with other findings concerning ageing. For example, Bouma<sup>1</sup> has shown that contrast sensitivity is a function of age, and that it diminishes from the mid-twenties onwards; Mann and Sharpley<sup>2</sup> have found there is a tendency for the rod field of the dark-adapted eye to contract with advancing age, this tendency becoming apparent at about the age of 30 years; and it has been shown that manual motility begins to decline in the late twenties<sup>3</sup>. Probably many accidents should be attributed to the slowing down of vision as age advances, and it is well known that dissatisfaction with standards of artificial lighting commonly found in workplaces is most prevalent among middle-aged and elderly workers. The general tendency for visual performance to decline from a fairly early age, which, in spite of the few subjects studied, is so consistently shown by the results presented in this paper, is certainly subject to individual exceptions. Indeed, individually, some of the subjects of these experiments showed different rates of decline, and probably began their decline at different, though not widely different, ages.

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## SIDELIGHTS ON THE INFERIOR OBLIQUE MUSCLE

BY

J. RINGLAND ANDERSON

MELBOURNE

#### ANATOMICAL FEATURES

The relationships of this muscle to the inferior rectus and to the capsule of Tenon and neighbouring orbital fascia require emphasis. These are assuming greater importance as the inferior oblique muscle is directly or indirectly concerned with an increasing number of surgical procedures. The connection between the sheaths of the two inferior muscles and Tenon's capsule restricts the effect of division of the inferior oblique muscle. The results of such an operation may vary with the intimacy of such connections and the strength of the check ligaments.

"English anatomists do not appear to have paid minute attention to this subject." So wrote Lockwood in 1886, 83 years after Tenon's discovery of the capsule that bears his name. If attention has been paid to it since, a perusal of the literature does not make a clear conception obvious. The following description based largely on dissections of refrigerated foetal material appears to the author as accurate (fig. 1).

Tenon's capsule is the membrane surrounding the globe from the limbus to the optic nerve. It varies in thickness, being thickest

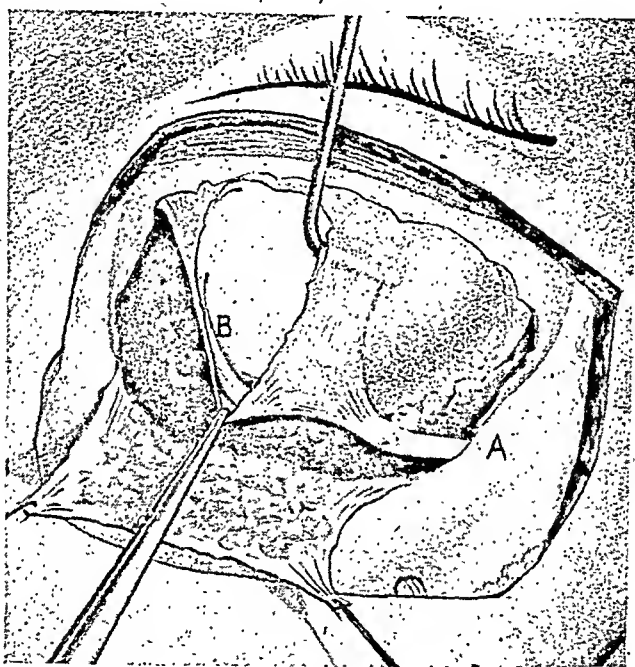


FIG. 1.

The septum orbitale has been opened, a portion of it is seen above, but it is mostly turned down over the zygomatic margin of the right orbit. Over this lies the superficial layer of fat. A portion of Tenon's capsule—the intermembrano is membrane between the inferior and external recti—has been excised exposing margins of these muscles and the insertion of the inferior oblique. The latter is uncovered as forceps draw downwards the suspensory ligament, with which is united the sheath of this muscle. Traction on this sheath shows its union with that of the inferior rectus.

The suspensory ligament is shown approaching its medial and lateral bony attachments. As it approaches the tubercle of Whitnall laterally, it is fused with the septum orbitale, the check ligament of the external rectus and the lateral palpebral ligament. The site for reattachment of the origin of the muscle in Wheeler's operation of advancement is marked by A. That for reattachment of the insertion in White's operation of recession is shown at B.

between the equator and the insertions of the muscles. In this area it is loosely attached to the globe by strands of episcleral tissue. In front it is firmly attached.

Each extra-ocular muscle is surrounded by a fine fibrous sheath. In front of the equator the sheaths of adjacent muscles extend towards each other, meet and fuse. These fused extensions form the inter-muscular membrane which encircles the globe in front of the equator. It is reinforced by overlying fibrous tissue.

The sheaths of the inferior muscles unite as they cross at right angles. They and the intermuscular membrane on each side are reinforced as it runs to join the medial and check ligaments at their insertions to the lacrimal and malar bones respectively. This reinforced portion was first described by Lockwood (1886), and is known as the suspensory ligament. The check ligament of the inferior rectus runs forward as a thin layer to the lower eyelid where it is attached between the tarsus and the overlying orbicularis oculi. The sheath of the inferior oblique, or according to Russell, 1948, its inferior layer, is continuous with the suspensory ligament as it runs up to its lateral attachment to Whitnall's tubercle on the zygoma. From the sheath of the inferior oblique a delicate strand of fibrous tissue runs laterally to be attached to the periorbita near the orbital floor. This, as Whitnall suggested, may be inconstant.

#### APPROACH TO ORIGIN OF THE INFERIOR OBLIQUE MUSCLE

The origin is adjacent to or rarely more than 5 millimetres from the incisura lacrimalis. The muscle passes laterally and slightly backwards between the inferior rectus and a layer of fat lying on the orbital floor.

One divides the orbicularis oculi and underlying septum orbitale down to the inferior medial border of the orbital margin where it runs obliquely upwards towards the lacrimal sac. If one inserts a muscle hook along the floor of the orbit, turns its point upwards, one engages the muscle and can draw it forwards. It may be necessary to separate it from fat for this ubiquitous packing lies on both its deep and superficial aspects. A myomectomy is performed by holding the muscle in artery forceps and removing the held portion by cutting on each side of the forceps.

As the inferior oblique muscle leaves its point of origin it is clad with a delicate sheath. It appears as if this muscle becomes attached by its sheath to the suspensory ligament, then runs below the inferior rectus and finally passes obliquely through Tenon's capsule into the space beneath it. This part of the capsule is the portion of the intermuscular membrane that joins the sheath of the external rectus along its lower border. Here the inferior oblique

muscle lies posterior to the suspensory ligament. The insertion into the sclera is oblique and about 10 millimetres in length, and lies in and below the horizontal meridian. It is under the external rectus, its anterior end being 2 millimetres above the lower level of the external rectus and almost 10 millimetres behind the insertion of this muscle. Fink, 1947. A subcapsular potential space surrounds the terminal portion of the inferior oblique muscle.

#### APPROACH TO INSERTION OF THE INFERIOR OBLIQUE MUSCLE

As the insertion extends to a point usually 4 millimetres from the fovea the first essential is to rotate the eyeball well upwards and inwards. It may be kept there by a scleral suture. After incision of the conjunctiva one may engage the short tendon below the external rectus before or, more simply, after division of this muscle.

Salzmann, quoted by Whitnall and Fuchs; quoted by Berens, 1943, stated that the line of insertion often showed gross irregularities, yet Howe, quoted by Krewson (1944), found its site almost constant. Fink, 1947, found insertional variations of the inferior oblique muscle to be second only to those of the superior oblique muscle. In one of his specimens the insertion surrounded the optic nerve. The sheath of the muscle sends extensions that usually join the sheath of the nerve and surround the posterior ciliary nerve and vessels.

#### FUNCTIONS OF THE INFERIOR OBLIQUE MUSCLE.

Though in opposition to Whitnall, Wolff and others it is reasonable to consider the primary action of the oblique muscles to be torsion rather than elevation or depression. This idea was stated by Maddox and Peters and has recently been clarified by Adler (1946). He considered that this muscle was 56.1 per cent. an extorter and 42.9 per cent. an elevator. It is of interest to recall the term "circumagentes" which was applied by anatomists to the oblique muscles up to the beginning of the 18th Century. Thomas Gibson in the 1688 edition of his "The Anatomy of Human Bodies Epitomized" wrote "The oblique muscles are called circumagentes, winders or rollers about, and amatorii, or amorous, and are in number two." John Brown in 1681 wrote, "These two muscles are called amatorii or the lover's muscles, being as the true messengers of affection, by some they are called circumactores or the rowling muscles, for they do much work in human body." Bartholin in 1655 and Porterfield in 1759 appeared to share this view, whilst Zinn in 1755 stated that their action was rotatory, but he used the modern titles. Dr. Kenneth F. Russell, who supplied me with this historical information, wrote "If you study a patient with a vertical coloboma when he fixes

his gaze on some distant object and then slowly move his head laterally—it will be noted that the coloboma will remain in the vertical plane for an appreciable period after the lateral movement has commenced. This amounts to about  $5-7^\circ$  and represents the rotation of the globe of the eye by the oblique muscles." See also Russell 1932. If we are correct in this view then there is a pair of muscles which primarily rotates vertically, horizontally and circularly or clockwise, respectively.

Though the majority of observers class the inferior oblique muscle as an abductor, Krewson (1944) recently drew attention to Volkmann's measurements which suggested that it was an adductor. He found that the muscle passed anterior to the vertical axis. The muscle is certainly in this position when the globe is rotated inwards. The diplopia in paralysis would be crossed in the extreme contralateral field if this were so.

The oblique muscles are certainly of less importance than the vertical recti in the vertical plane. The superior rectus is 73.7 per cent. effective as an elevator and the inferior oblique muscle, but 42.9 per cent.

As is well known the inferior oblique muscles, when the eyeball is in adduction, are frequently found to act in excess as elevators. This may be due to a variety of causes.

### Overaction of the Inferior Oblique Muscle

*Causes.* These have been discussed in detail elsewhere (Anderson, 1942). Here it is sufficient to classify possible causes as follows:—

(1). Primary overaction due to either asymmetry in the balance or in the insertions of the superior and the corresponding inferior oblique muscles, or to deficient fascial check ligaments or to an oblique insertion of the internal rectus. The presence of an accessory inferior oblique muscle (Whitnall) may explain overaction. Possibly excessive adhesions between the inferior oblique and the inferior or external rectus may act similarly. Chavasse appeared to consider this apparent imbalance in adduction between the oblique muscles to be the rule. It is wise, therefore, to compare the features of these two muscles. See Table I.

Reference to this comparison shows that the superior has less vertical purchase than the inferior oblique muscle, because its tendon makes an angle that is  $4\frac{1}{2}$  degrees greater with the median plane than does the inferior oblique muscle. Berens (1936) quoted Verrijp who claimed that the inferior contributed more of its energy to elevation than does the superior oblique to depression as 42 per cent. is to 37 per cent.

TABLE I

Muscle	Nerve Supply	Action, Main and Subsidiary	Length of Muscle and Tendon	Check Ligament, Attachment	Origin	Insertions which are Variable	Arc of Scleral Contact	Plane of Action	Energy used in Vertical Rotation	Paralysis
SUPERIOR OBLIQUE MUSCLE Origin 2nd Somite	IV	Intorsion, Abduction, Depression.	Both longest	Close to vertical meridian, attached to superior rectus	Posterior	Posterior at 45° to transverse axis. Within 7.5 mm. of optic nerve	Very small	55° 21' from median plane	37%	2nd most frequent
INFERIOR OBLIQUE MUSCLE Origin 3rd Somite	III	Extorsion, Abduction, Elevation.	Shortest muscle though longer than "effective" part of S.O. No real tendon	Attached to inferior rectus and to orbital margin	Anterior even to pulley of S.O.	In horizontal meridian at 25° to line of S.O. insertion. Within 4.0 mm. of optic nerve	Large	50° 57' from median plane	42%	Rarest, may be associated with internal paralysis

(2). Overaction secondary to paresis of the homolateral superior oblique or the contralateral superior rectus. Overaction is particularly likely to occur in the former condition if the paretic eye is used for fixation. Verhoeff (1941) considered that overaction was always due to paresis of the superior oblique muscle or to hypoplasia of the trochlear nucleus.

There are two schools of thought each based on a difference in method of diagnosis. Each school blamed a different superior muscle paresis as the common cause of overaction. White and Brown (1939) following Duane found weakness of the superior rectus 28 times more frequently than that of the superior oblique muscle. Bielschowsky and his followers believed that paresis of the superior oblique was the most frequent ocular palsy.

The overaction is due, on the one hand, to lack of opposition from the paretic antagonist, the superior oblique muscle, and on the other hand to excessive stimulation following paresis of the yoke muscle, the opposite superior rectus. As Adler (1946) pointed out, part of the disagreement is due to some authors considering only primary paresis (*e.g.*, Davis, 1944), while others paresis associated with horizontal strabismus as well (White and Brown). Adler found that an isolated primary vertical palsy as studied by Davis (1944) was more commonly of the superior oblique muscle, but that the vast majority of vertical palsies associated with strabismus, as studied by White and Brown, was probably due to a weakness of the superior recti.

In my first series of 127 vertical ocular palsies accompanied by horizontal strabismus the superior rectus appeared to be at fault in 56 per cent. and the superior oblique muscle in 33 per cent. of cases. In my second series of 54 vertical ocular palsies the superior rectus was affected in 48 per cent. and the superior oblique muscle in 27 per cent. when accompanied by horizontal

TABLE II

PARALYSIS	— Sup. R.	— Sup. O.	— Inf. R.	— Inf. O.	TOTAL	
With horizontal strabismus	56%	33%	7%	4%	82	1st Series
	48	27	18	6	33	2nd Series
Isolated vertical squint	70	27	2	2	45	1st Series
	57	33	5	5	21	2nd Series

NOTE. In addition there were 16 cases in which the inferior rectus and the contralateral inferior oblique were affected and diagnosis of the initial lesion was not made.



TABLE III

MUSCLE DEFECTS																
DISORDER	+Inf. O.				-Inf. O.				- Inf. R	R&L Inf. O and R&L Inf. R	- S.R			- S.O		
	No H.D.	R	L	R&L	R	L	With - Inf. R	R			L	R&L	R	L	R&L	
ALT. C.C.S.	2	4	2	3	—	—	1	—	—	1	—	—	—	—	—	
Right C.C.S.	19	11	2	8	—	1	3	2	—	4	—	—	1	3	—	
Left C.C.S.	31	10	16	11	—	1	2	1	1	1	4	2	—	4	1	
DIVERGENCE	7	6	4	1	—	—	2	3	2	1	6	—	—	1	—	
Isolated Vertical Squint	—	—	—	—	—	1	—	1	1	3	8	—	3	4	—	
TOTAL	59	31	24	23	—	3	8	7	4	10	18	2	4	12	1	

Eight cases of paralysis of a lateral rectus and five of true or approximately true hyperphoria were included. Fifteen doubtful cases were excluded.

GRAND TOTAL 219 cases with horizontal or vertical strabismus, parietic and so-called concomitant.

67 cases or 30% had no vertical defect.

78 cases or 36% showed an overaction of one or both inferior oblique muscles that was the only vertical defect.

In 47 cases or 22% the overaction appeared to be secondary to another vertical defect. Three times this was bilateral and associated with palsy of both superior recti and once with bilateral trochlear palsy.

In 3 cases inferior oblique palsy was unilateral, in 8 cases it was associated with weakness of the opposite inferior rectus and the initial palsy was in doubt.

In 4 cases this condition was bilateral and in 7 cases the inferior rectus was paresed.

strabismus. As isolated palsies the superior rectus was affected in 57 per cent. and the superior oblique in 33 per cent. See Tables II and III.

#### RECOGNITION OF OVERACTION.

The overaction may be of the first degree, that is present on ordinary adduction, or of the second degree, present only on forced adduction or of the third degree, that is present only when the eye is looking upwards as well as inwards.

Vertical errors in ocular alignment are not easy to recognise if slight, or if associated with high degrees of convergence or divergence. Reliance on features that may be used for reference such as margins of lids and the distance from them to the pupils may be misleading. The lids may be asymmetrical. A palpebral aperture updrawn laterally below an abducted eye or down-drawn medially below an adducted eye may suggest elevation of the

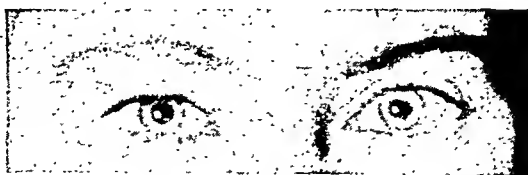


FIG. 2.

An apparent right hypotropia due to the lower level of the right orbit. The true angle was 7 dioptres of right hypertropia. The cause was probably a paresis of the left inferior oblique.

adducted eye. So often facial asymmetry if not congenital soon appears as a testimony to the strain of life. The cover test is always the safest guide. One eye or even the orbit may be at a different level, and unless recognised may lead to faulty diagnosis

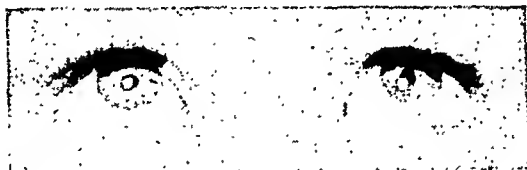


FIG. 3.



FIG. 4.

Retraction syndrome showing elevation excess on attempting adduction of left eye.

and surgical bewilderment. This was so in the following case :— Dorothy A. showed - LIO, - RIR, +RSR, +LSO, by the screen test and the torticollis present suggested that the original lesion was paresis of the left inferior oblique muscle. Prior to this test, however, it was considered that there was a right hypotropia. This was due to the right eye and orbit being on a lower level than the left. There were really 7 dioptres of right hypertropia at a resting angle of -2. See Fig. 2.

Faulty diagnosis was the main reason why eight separate operations were necessary in a patient reported in a recent copy of the *American Journal of Ophthalmology*.

The excessive elevation on attempted adduction in the retraction syndrome is still a mystery. Figs. 3 and 4 are of a boy with absent adduction and abduction and a slight left hypertropia (3). On attempting adduction the left cornea disappeared under the lid (4). Myomectomy of the inferior oblique was performed twice and the superior rectus was receded without reduction of the elevation excess.

#### TREATMENT.

"A single oblique overaction if strong often necessitates an operation to weaken the muscle. The double oblique overaction can often be ignored provided that it does not interfere with the patient's binocular vision." Sheila Mayou, 1947.

(1). Tenotomy or myomectomy near the origin has been the most common operation. The approach may be cutaneous or conjunctival. It is simple to perform but has certain disadvantages. (1) The result is variable. Very often, however, one has been surprised because the result was so accurate, corresponding with the correction one wished. This was probably so, because the need for correction and the effect of a standardised operation would both vary directly with the degree of overaction present. But because the result has been occasionally, (1) insufficient (Dunnington, 1942; Gifford 1942), (2) excessive (White, 1942), or (3) complicated by cyclotropia (Berens, 1942), there is a tendency to follow White's lead and recede the muscle at its insertion.

Gifford wrote that to prevent reattachment near its origin it was wise to resect 4 millimetres to free the muscle completely from fascial attachments. Otherwise he found that the muscle tended to become reattached near its origin. Neely, 1947, preferred a tenectomy near the origin, and if necessary a tenotomy at the insertion later.

(2). Tenotomy at the insertion. This operation leads to variable results (White 1942) and others, or "almost invariably complete paralysis" (Dunnington, 1942).

(3). Recession, at the insertion as described by White (1942, 1944) and later by Guibor (1944), leads to "much more definite and accurate means of control." Though myomectomy near the origin is usually satisfactory for a unilateral hypertröpia over 15 dioptries, in smaller unilateral errors and in bilateral cases recession is indicated. The fibrous bands between this muscle and the

external rectus require division White (1942). In addition, Guibor (1944), advised division of bands between the inferior oblique and inferior rectus unless one was performing a tenotomy in which case a paralysis would result. The wisdom of dividing them in a recession is doubtful. Berens, 1942, stated that it was not known yet how far to recede the muscle. The tendency was to under-correct the error. He receded the muscle 9-10 millimetres and as much as 7 millimetres without detaching the external rectus. He had obtained from 4-6 dioptres to total correction of 18 to 20 dioptres. He thought that a recession of 8 millimetres would correct from 5 to 8 dioptres in the primary position. He described a reduction in esotropia when present from one-third to one-half; in one bilateral case it was from 18 to 5 prism dioptres. White severed the muscle 2 millimetres from the insertion. It has been stated that undue trauma could produce choroiditis near the macula and as a paracentral scotoma. Dunnington. The posterior vortex vein, which is 5.5 millimetres behind the equator, is anterior and medial to the insertion. Care must be taken to avoid the inferior rectus muscle.

Stallard (1946) described a recession controlled by 2 mattress sutures through the ends of the divided muscle. Prangen (1947) attached the inferior oblique tendon on the horizontal meridian and 6-7 millimetres posterior to the mid-point of the insertion of the external rectus. This, he claimed, eliminated all elevation, in adduction.

(4). Altered insertions of the horizontal rectus muscles. Bielschowsky, 1945, corrected a high degree of overaction by lowering the insertion of the ipsilateral internal rectus. Foster & Pemberton, 1946, found that the eye tended to move in the direction of the displacement of the insertion. Half-width raising and resection of the external rectus gave on an average 5.4 dioptres and half width raising of the internal rectus gave half this amount. They considered that marked shortening of the muscle increased the vertical effect.

If the superior oblique was paralysed Wheeler (1935) and later White (1944), sometimes preferred a tuck or advancement, and McGuire (1948) preferred a resection of the paralytic muscle to weakening of the overacting inferior oblique muscle.

### Underaction or Paralysis of the Inferior Oblique Muscle

Bielschowsky found that paralysis was extremely rare. The incidence as found by others is summarised below:—

TABLE IV

Incidence among	Authors	Series	Sup. R.	Sup. O.	Inf. R.	Inf. O.
Congen. Vertical Motor Pareses	White & Brown, 1939	661	Per cent. 75	Per cent. 2	Per cent. 18	Per cent. 3
	Duane, 1912	107	54	7	33	6
All Ocular palsies	Tomizo, 1936	150	3.3 Ext. R.	10.7 29.3	3.3 Oculomotor	0.7 43.3
Unilateral Vertical palsies	Anderson, 1st series-1947	150	53	27	11	9
	2nd series†	62	45	26	11	5
	Hughes, 1943	47	39	6	1	4
Traumatic Ocular palsies	Cross, quoted by Neely	138	24 Ext. R.	21.5 11	2 Int. R.	6 5
	Neely, 1947	54	26 Ext. R.	31 41	4	—

† NOTE. In this series there were 8 cases with weak inferior rectus and inferior oblique muscles and the initial lesion was not known.

Paresis of the inferior oblique muscle may occur as an isolated palsy when it may be congenital or acquired, or it may be associated with other palsies.

#### ASSOCIATED PALSY.

1. It may be associated with weakness of the contralateral inferior rectus. In paralysis of either muscle a secondary underaction, so called "inhibitional paresis," of the other may occur. If the R. Inf. O. be weak, the ipsilateral antagonist, R.S.O. contracts because of weakened opposition. A reduced stimulus is then required for a given action. Therefore the yoke muscle, L. Inf. R. also will receive a weak stimulus and so appear paretic (Adler, 1946). Just as difficulty in recognising the initial lesion is found in associated paresis of the opposite superior oblique and rectus muscles it also occurs, but less frequently, in disentangling weakness of the inferior oblique and of the opposite inferior rectus muscles. The same guides fortunately hold here. They are:—

- (a) Torticollis is more likely if the oblique muscle is affected.
- (b) Increase of vertical deviation on forced tilting of the head to the opposite side occurs if the oblique is weak.
- (c) The smaller field of fixation usually belongs to the eye with the primarily affected muscle.

2. Inferior oblique paresis may also be associated with paresis of the homolateral inferior rectus. When we recall their intimate relationship especially in development this is not a surprising occurrence. Chavasse, 1939.

3. Paresis of the inferior oblique muscle and the homolateral superior rectus may occur together. No elevation of the affected eye will be present. According to White (1942) and Burian (1942), this association is not infrequently seen. The inferior oblique muscle is usually the more parietic.

4. Paresis of the inferior oblique may be associated with that of the medial and the inferior rectus, if the inferior division, and with the superior rectus if both divisions of the third nerve are affected.

5. Paresis of both inferior oblique muscles. This is usually accompanied by underaction of both inferior recti. In my first series this condition was found twice and four times in the second series. Hughes (1943) found paresis of both inferior oblique muscles in one of sixty-nine patients with vertical palsies.

#### ISOLATED PALSY.

It is the least common isolated oculomotor paralysis (See Table IV).

##### 1. *Congenital Causes.*

These have been summarised recently (Epstein, 1947). There may be:—

- (1) Errors of cleavage. The inferior muscles do not completely separate from each other till the 20 millimetre stage.
- (2) Aplasia of primitive head cavities.
- (3) Aplasia of connections within the central nervous system.

##### 2. *Traumatic Causes.*

Paralysis of the inferior oblique muscle is very rarely the result of the usual forms of trauma. Its production at operation however is possible. The inferior oblique muscle may be injured accidentally during operations for retinal detachment and Gifford's case 22 (1942), is an example of this. White (1943) warned against a similar injury during a recession of the external rectus. This is more likely to occur if this muscle has been operated on previously. It has been claimed that hypertopia following such an operation may be due to such an injury.

#### TREATMENT.

The successful methods of treatment may be summarised as follows:—

### 1. *To Strengthen the Affected Muscle.*

(a) Advance at bony origin. Wheeler 1935, Kirby 1946, preferred this and reported cases. Chavasse thought this was the wisest treatment. With the courage based on accurate observations that characterised him, J. M. Wheeler led this attack on the paralysed muscle itself. He advanced the muscle over the orbital margin and using two sutures attached it to the periosteum of the maxilla. He obtained satisfactory results, 1935. He and White agreed, however, that in paralysis this alone was inadequate.

(b) "Advance" or tuck at insertion and if inadequate perform recession of contralateral superior rectus. (White, 1942, 1943, 1945; Dunnington, 1942). White, however, stated that neither splicing at the insertion nor tucking at the origin gave as large a correction as Wheeler's operation which could correct from 30° to 50° according to which eye was fixing.

(c) Resection at insertion. Berens and Loutfallah (1943) used a single mattress suture. Wagman (1945) preferred three sutures.

### 2. *To Weaken Contralateral Yoke Muscle.*

(a) Duane suggested tenotomy of the contralateral superior rectus.

(b) Recession of this muscle was used by Kirby (1946), Dunnington (1929), Berens, Paine and Kern (1935), Sheppard (1947), and others. Berke claimed that this operation might widen the palpebral aperture and unduly restrict elevation.

### 3. *To Weaken Homolateral Antagonist Muscle.*

(a) Tenotomy of homolateral superior oblique. Dunnington stated that it was not feasible to weaken this muscle and White thought he had never seen an indication for its tenotomy. Berke (1947), however, claimed that this was the best treatment for overaction of the superior oblique muscle.

(b) Recession of trochlea. Hughes (1944) and Hughes and Bogart (1942), reported 8 cases. Wagman (1945) thought that though their cases were mainly due to overactive superior oblique muscles, the initial lesion in some was probably paresis of the inferior oblique.

### Conclusion

Careful dissection, a study of function, and accurate clinical observation must precede accurate diagnosis and without accuracy in diagnosis satisfactory treatment is unlikely. The significance of slight errors in ocular movements is obscure. They do not all mean a previous lesion or even a minor rôle in producing strabismus. Their frequency in normal cases is as yet unknown.

The underaction of a contralateral antagonist may be diagnosed

as a primary lesion and the initial paresis missed or given a secondary rôle. This applies to a superior or inferior rectus and its corresponding opposite superior or inferior oblique muscle. As my observations increase my diagnosis of palsy of the superior rectus appears less frequently. Its frequency fell from 53 per cent. in my first series to 45 per cent. in my second series. One must be careful in diagnosing it (1) unless associated with ptosis or weakness of another muscle supplied by the third nerve, (2) if torticollis to one shoulder is marked and increases on tilting the head to the opposite side, or (3) the projection field of the suspected eye is smaller than that of its fellow.

One must be careful to correct large horizontal errors before tackling most vertical defects. The latter may become negligible or require only an unilateral operation. Sometimes after an operation on one overacting inferior oblique, if both had been overacting, there may be an apparent increase in the overaction of its fellow.

It may become possible to vary reattachment to correct sometimes more torsion and sometimes more elevation according to the particular need of the patient. Wheeler, 1935, in shortening the superior oblique muscle reattached it farther forwards to correct torsion, and backwards to correct elevation.

I would express my gratitude to Dr. H. F. Bettinger of the Women's Hospital, Melbourne, for supplying material for dissections, to Dr. K. F. Russell of the Department of Anatomy, Melbourne University, for advice and help with these, and to Rev. W. M. Rolland for his skill and patience in drawing.

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## SOME UNUSUAL CASES OF SJÖGREN'S SYNDROME

BY

HOWARD COVERDALE

AUCKLAND

SJÖGREN'S syndrome indicates a general constitutional or systemic disturbance of unknown origin. Very complete investigations of typical cases have been made by Sjögren, Bruce, Lutman and Favata and Stenstam without finding any common aetiological factor, and all that can be said is that most cases appear in women at or after the menopause without any history of previous disturbance of the menstrual cycle.

In this regard it is well to bear in mind the extreme chronicity of the complaint and the possibility of the menopause being only an aggravating factor in a condition already established. The most striking impression gained from reading the details of published cases is the freedom of the patients from any disorder not referable to the syndrome described by Sjögren.

It is of interest, therefore, to record cases with unusual constitutional features, and numbers one and two described below are of a man and his daughter, the latter with a lifelong history of dry eyes and showing signs of pituitary dysfunction. The third and fourth are of a woman and her daughter, the latter having pulmonary tuberculosis. The fifth case is of a young woman whose symptoms seemed to originate from a fracture of the base of the skull.

**CASE 1.**—Because of a feeling of grittiness in his eyes and some hypersensitivity to light of many years duration, Mr. A., aged 68 years, had had a habit of sitting with his eyes closed when not at work. During this time he had also had slight dryness of the mouth. He made no complaint of these disabilities until a few months ago when he had a cerebral haemorrhage with hemiplegia and his eyes became worse.

He was found to have typical filamentary keratitis with a Schirmer's test of 5 mm. in 5 minutes (control, 25 mm.). The filaments and much of the discomfort disappeared in a few weeks with no more than the application of vaseline to the lid margins, though the deficient lacrimal secretion remained unchanged. The corneal sensitivity was normal. There was no history of enlargement of the parotid glands, and any rheumatism had been slight.

A diagnosis of keratitis sicca may be preferred to that of Sjögren's syndrome, and there is only his previous tendency to sit with the eyes closed to indicate that the condition preceded the cerebral haemorrhage.

**CASE 2.**—Miss G.A., aged 36 years, the daughter of Mr. A., above, said emphatically that even when crying she had never known a tear to come from either eye. Any irritation such as from foreign bodies had caused only a stinging sensation without lacrimation. Her mother stated that even as a child her daughter's eyes had been chronically sore and intolerant of light, and no tears had formed.

She came under observation 10 years ago at the age of 26 with chronic conjunctivitis, mucoid threads and myopia. A year later, in 1939, she consulted her physician, Dr. E. J. Fischmann, for amenorrhoea and a very large number of boils. She had been having severe headaches, sometimes with vomiting, and her size of shoes had changed from 5 to 7 with a proportionate enlargement of the hands. A roentgenogram of the sella turcica was thought to show some enlargement, but the fields of vision, blind spots and discs revealed no abnormality.

At this time Dr. Fischmann demonstrated the pituitary symptoms and signs to the Auckland Clinical Society. These consisted of obesity of a typical hypopituitary type, amenorrhoea, loss of hair on the scalp, growth of hair on the face, a tendency to kyphosis, striae distensae, slight exophthalmos, polydipsia, albuminuria and increased blood pressure. In addition and in contradiction to this picture of pituitary basophilism, she also had acromegaly.

Three months later, a small loss of peripheral field was detected down and out in the right field and up and out in the left. The blind spots and discs remained normal. The pituitary gland was then explored by Sir Carrick Robertson, but no tumour was found.

Shortly after the operation, the eyes became gritty and inflamed and showed fine superficial keratitis, chiefly of the upper half of each cornea, with slight pitting and fine scattered epithelial spots, many of which stained with fluorescein. Mucoid threads were present. Sensitivity was normal. About this time the mouth began to feel dry, and swelling of the parotid glands was first noticed. During the next eight months she was examined on several occasions without any material variation in the signs, though the degree of discomfort was very variable.

Service with the New Zealand Division abroad prevented further examination by the writer for some years, but, after the war, there was no doubt that she presented the typical features of Sjögren's syndrome. The corneae showed the same changes as before with, in addition, slight limbal vascularisation and some small filaments. Mucoid threads were present and Shirmer's test showed no absorption beyond the lid margin from either eye in 5 minutes (control 30 mm.). The discs were normal and the only field defect was a partial right centro-caecal scotoma. The mouth was dry and the parotid glands were considerably enlarged and tender. There was a history of rheumatism and the menstrual periods had not returned. She stated that she had seldom perspired and then only slightly.

There was no radiographic evidence of salivary calculus and the sella turcica was of normal size with intact bony outlines. The Kahn test was one plus positive and the Wassermann reaction doubtful on two occasions. At a third examination the Wassermann reaction was one plus positive. The blood count and sedimentation rate showed no abnormality.

In a personal communication, Dr. Fischmann gives the following additional information:—

"Involvement of the joints was observed on two occasions. In 1945, moderate pain and swelling of the proximal interphalangeal joint of the right middle finger appeared, accompanied by ache in the calf muscles, especially during the night. X-ray of the involved joint proved negative. In 1947, pain appeared in the knees, wrists and ankles with slight swelling of the ankles and the right thumb base joint.

The joint involvement does not conform with any of the three classical patterns of chronic joint disease (rheumatoid arthritis, osteo-arthritis and gout). It resembles the palindromic rheumatism of Mayo Clinic investigators more closely than any other joint disease known to me.

To test pituitary function, an insulin tolerance test, the basal metabolic rate and a water concentration and dilution test were done in 1945. These tests as well as an electrocardiogram were normal.

Would you think that the early cessation of ovarian function due to absence of the two gonadotrophic pituitary hormones may have played a rôle in the early onset of keratoconjunctivitis sicca?"

As the patient is intelligent and there is no reason to doubt the accuracy of the history it is probable that this is a case of Sjögren's

syndrome of congenital origin analogous to Duke-Elder's case of congenital keratoconjunctivitis sicca, and a case recorded by Hamilton. In the present state of our knowledge it is impossible to say what significance, if any, can be given to the pituitary dysfunction or the doubtful Wassermann reaction.

**CASE 3.**—Mrs. S., aged 58 years, complained of a varying degree of soreness of the eyes of about four year's duration. Various kinds of drops had been prescribed by her physician, but they had all been irritating and she had found by experience that the best remedy was frequent bathings with water. On being questioned, she stated that the mouth had been dry, the saliva frothy and the tongue at times inflamed for about eight years. The inflammation of the tongue had responded to treatment with vitamins. The parotid glands had been swollen and tender on three occasions in 1946. She had had her teeth removed about fifteen years ago and had not had any rheumatism.

On examination, the eyes showed the characteristic changes of keratoconjunctivitis sicca with a few fine filaments and a mild degree of staining with fluorescein. Shimmer's test showed only 2 mm. of moistening in each eye on two occasions.

The patient lived in a remote town and it was not possible to have any pathological investigations made.

**CASE 4.**—Miss M.S., aged 26 years, daughter of Mrs. S., case 3, was seen for the first time this year. She complained that her eyes had been chronically inflamed and sore in varying degrees for about four years. When questioned, she said that she could not remember ever having noticed any tears, that her voice had been husky for a few years and that, during this time, she had had slight dryness of the mouth in the mornings and a tender swelling of the parotid glands every month or two. This swelling had usually lasted only a few days and had twice been diagnosed as mumps. Her teeth had decayed at an early age and had all been removed when she was 17. Perspiration had always been free on the hands and feet, but not elsewhere. Her menstrual periods had been and still were quite normal.

As a child, she had been suspected of having pulmonary tuberculosis. This was confirmed in 1944 and she was admitted to a sanatorium, and, although the infection was under control, she still had a pneumothorax. Her health otherwise had been good except for slight rheumatism in the arms and legs. Her father had died of tuberculosis and her two sisters were affected. Two brothers were healthy.

She was a tall, round shouldered girl of unemotional temperament whose only obvious disabilities were her chest and her inflamed eyes. The characteristic mucoid threads of keratoconjunctivitis sicca were present, the corneae showed superficial keratitis chiefly in the upper halves and, when stained with fluorescein, showed much superficial punctate staining and many fine mucoid filaments. The vision was reduced by the keratitis to 6/9 in the right eye and 6/24 in the left. There was no intra-ocular abnormality. Shimmer's test showed an absorption of 4 mm. in the right eye and 3 mm. in the left in 5 minutes (control 30 mm.). The corneal sensation was normal.

The Wassermann reaction was negative and the blood examination revealed an increased sedimentation rate and such other changes as would be expected in a case of tuberculosis.

**CASE 5.**—Miss M.W., aged 33 years, met with an accident at the age of 21 in which the base of her skull was fractured, with consequential paralysis of the right side of the face, paralysis of the right external rectus muscle and deafness of the right ear. Except for diplopia, the vision was unaffected. When she recovered full consciousness she found that her mouth was dry, and she has been unable to eat dry foods ever since.

The facial paralysis recovered in about six weeks, but the external rectus paralysis, the deafness and the dry mouth have persisted.

A few months after the accident her teeth began to decay, her nose and throat became dry so that she had to gargle every morning, the saliva became thick, white

and scanty, and the tears did not form normally. The eyes, however, remained comfortable and free of inflammation.

About four years later the left eye became chronically inflamed and gritty and tended to close, especially in a strong light. When irritated, both eyes smarted but no tears formed. Mucous threads were sometimes present in the mornings.

Except for some slight enlargement of the thyroid gland at about the age of 17 her general health has been good, her menstrual periods have been regular and she has had no abnormalities of the skin and no rheumatism. The parotid glands have not been enlarged. Since the accident, however, her memory has been poor and she has had a persistent feeling of drowsiness.

On examination, she was found to be of healthy appearance and of unemotional temperament. The teeth showed very extensive repair. There was some chronic conjunctivitis, chiefly of the left eye, and both corneae showed fine superficial erosions staining with fluorescein. Shirmer's test revealed:—Right eye, 10 mm. of moistening, left eye, 6 mm., normal control, 30 mm. The differential blood count, sedimentation rate and Kahn test were normal.

The sella turcica was normal in shape and size and its bony outlines were well defined, regular, and intact. There was no radiographic evidence of the old fracture of the skull.

### COMMENT.

Some of these cases illustrate a common and understandable vagueness about the time of onset. The progress is usually extremely slow and there is a considerable difference between the result of Shirmer's test in the normal subject and in the patient with signs and symptoms of keratoconjunctivitis sicca. A patient may show the syndrome in a fairly advanced state without being greatly inconvenienced and it is usually impossible even to infer when secretion began to fail. Sjögren has pointed out that the organic changes in the gland appear earlier than the symptoms of diminished secretion.

Case 5 may be analagous to Wagenmann's mentioned by Duke-Elder. The history of xerostomia soon after the fracture of the skull is unusually definite, but it is noteworthy that the symptoms in case 2 increased after the craniotomy for pituitary tumour.

In speculation as to the cause of the syndrome, allowance must be made for the possibility of commencement of the pathological process long before the first complaint of symptoms.

The doubtfully positive Wasserman reaction in case 2 and the tuberculosis in case 4 suggest infection as a causative factor. This is supported by the case of a man of 60 recently referred to the writer by Dr. A. N. Talbot. He had keratoconjunctivitis sicca with slight aqueous flare in both eyes and a posterior synechia. His Wassermann reaction and chest roentgenogram were negative. These, however, are isolated instances the significance of which must not be overestimated. It is more reasonable to suppose a congenital defect which may be made manifest at any period of life by some aggravating circumstance. This suggestion is supported by Lisch's series in which twelve people in three generations of one family showed some evidence of the syndrome.

Lisch states that the majority were of asthenic physique and looked ill, and Lutman and Favata mention the slender build and nervous temperaments of their cases. All those mentioned in this paper and four others under treatment at the present time are phlegmatic rather than excitable and, excepting case 2 with pituitary dysfunction, cannot be said either to be of any constitutional type or to look ill.

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## ADAPTATION TO ENVIRONMENT

BY

F. A. WILLIAMSON-NOBLE

LONDON

It has been a practice, especially during the war years, to analyse the job, to analyse the men, and to attempt to fit the right man into the right job. It is thus assumed that certain people have characteristics which enable them to develop along one particular line, and that along this line they will do better than along any other. Newton has taught that action and reaction are equal and opposite in the physical sphere, and to a limited extent the same may be true in the psychological. In other words, although the man has an effect on his work, his work also has an effect on him.

The majority of us become ophthalmic surgeons in rather a haphazard fashion; in fact, the same may be true of the whole medical profession, and it is more than likely that its members represent a random sample of the upper middle classes, it being only occasionally true that anyone goes into the medical profession because he has a particular flair for it, or thinks that he has.

If this be true, it is rather extraordinary that such a large percentage of doctors make good, and that there are not a greater number of square pegs in round holes. It is true, however, that there are some and that in the course of time the sharp edges get worn by the cylindrical circumference of the containing environment. Are we all worn into more or less the same shape by 15 to 20 years of ophthalmic practice, and if so, what characteristics may one justifiably look for in an ophthalmic surgeon of some years' experience?

To take first things first, let us consider the environment in which the ophthalmic surgeon finds himself. The estimation and correction of errors of refraction form a large part of his work, and considered as "work" it cannot escape the indictment of "monotony." Monotony in work, however, is what a large proportion of humanity perhaps unconsciously desires, since to do one thing really well is a source of deep satisfaction. The writer well remembers a conversation with one of the first Labour Members of Parliament, in which he asked whether monotonous work was not one of the bugbears of those who labour in factories. He received the unexpected reply, "by no means, the work can be done mechanically and without conscious effort so that it sets the mind free to think about what it likes." In the case of the Labour member the sonnets of Shakespeare were instanced as one of the things over which his mind liked to roam, and in the case of the eminent oculist whom this issue of the Journal commemorates, it is perhaps permissible to suppose that though the sonnets of Shakespeare were at times in his mind, other questions such as intricate problems in optics, pathology, colour vision and psychology entered and were perhaps resolved. The elderly Labour member supported his contention by instancing the owner of a factory who felt compassion for his workers on account of the monotony of their tasks, and by the exercise of considerable ingenuity arranged matters so that each man would have a change of work every week. What happened was that after a fortnight he was faced with the prospect of a strike if he did not return to the old method!

Monotony may thus have its merits, and although a large part of our consulting work may be almost mechanical, we contrive to make it interesting by seeing to how high a pitch of accuracy we can raise our efforts to correct what is in reality a mistake on the part of Dame Nature, that stern old autocrat whom we alternately woo, in hoping she will provide healing after a cataract operation, and defy in removing a lens she has allowed to become prematurely opaque.

There is another aspect of refraction work, however, which cannot fail to have an effect on those who practise it, and this is that

our patients are being constantly placed in a dilemma, and whether they like it or not, must give a definite answer "better, or worse or the same." It has been related that Frenchmen say "two and two make four," whereas the Englishman prefers to state that "no one can contradict me if I say that two and two do not make five." These two attitudes of mind are continually found in our patients, and it must be instructive to the oculist to compare the answers to the same series of questions by, say, a fresh, uninhibited child of five or six with those of an aged diplomat or a prominent industrialist. Here again we may surmise that the critical faculty and insight into character which are such prominent features of him whom we commemorate in this issue, may have been fanned into activity by these experiences.

Another aspect of refraction work is the opportunity it gives of observing at close quarters the features, facial expression and general demeanour of a large variety of different types of human beings. The patient is so engrossed in looking at the letters that he or she is unconscious of anything else, and can be observed in a state of complete detachment. Most of the observations are trivial, as, for example, that very few people fail to possess enlarged pores in the skin of their nose, though they are often filled with face powder, and look all the worse for it; but now and again the twitchings of the lids, the restless movements of the hands, and so on will give a clue to the underlying neurotic cause of the headaches. It is not given to many members, even of the medical profession, to have the opportunity of fifteen minutes or so undisturbed observation of preoccupied individuals at close quarters, and several years of this engrossing occupation must have an effect on the mental outlook of the observer.

Alertness of another type is also called for if more important defects are not to be missed. To give but one example, the failure of a patient to read the last few letters of a line of test type with the right eye, and the first few with the left eye may indicate a bitemporal hemianopic scotoma, which calls for further investigation. The same alertness, or an even higher degree of it is called for in ophthalmoscopic examinations.

In fact, the oculist must often feel that his professional life is, so to speak, a constant one man "Brains Trust" with Dame Nature as the question mistress, waiting to catch him out if he fails to notice what may at first sight appear to be unimportant signs and symptoms.

Emphasis should perhaps be laid on the one man aspect of this struggle, since the oculist is a Caesar, in the sense that there is no appeal to a higher authority except in the rare instances when a second opinion can justifiably be sought. He is thus taught to



accept and eventually to welcome responsibility and the tendency to "pass the buck" which is probably inherent in most human beings is, we hope, suppressed. Carried too far, this acceptance of responsibility may develop into tyrannical authoritarianism, but such a state is happily rare, its occurrence being prevented by the failures and disasters which inevitably happen to all of us.

When it comes to operating, some new factors have to be considered. It occurred recently to the writer to wonder why patients behaved so much better now than they did twenty years ago. Various answers suggested themselves, such as pre-medication with sedatives, facial nerve block and so on, but it was not until some time had elapsed that he hit on the true answer, which was, that it was not the patients who were behaving better, but he himself. The ability to impart such a degree of confidence in another human being that he or she will permit of the performance of an operation on the eye, even though it be analgesic, is a wonderful possession and is not lightly gained. It demands on the part of the operator not only mental and physical fitness, but a degree of confidence in his ability to do what he sets out to achieve, and the possibility of communicating this confidence to his patient lying supine on the table before him. The same communication of confidence is important during convalescence. An extreme example of this occurred to the writer when he had to perform a cataract extraction upon a devout Roman Catholic priest, who was so convinced that divine aid would be forthcoming that he knew he had no cause for anxiety. In consequence of this, he lay in bed tranquil and relaxed after the operation, to such good effect that it was difficult to say after a week which was the aphakic eye, and the second eye was then dealt with, with a similar result.

Some more points remain in considering the environment of the ophthalmic surgeon. The first is the high percentage of success he achieves in the treatment of his patients. This tends to make him a therapeutic optimist as opposed to the nihilism which affects some of his medical colleagues and possibly to be over credulous as to the value of certain forms of treatment. He may mistake for organic cure a result which is in reality due to suggestion, but the main thing to him is that the patient is better, whatever the means by which this has been achieved. An example which occurs to one's mind is the cure of chronic dyspepsia by the correction of small degrees of astigmatism. Another point is that most of the operations he performs have results, which are sudden and dramatic and may completely change the further outlook and potentialities of the patient; small wonder then that the oculist should receive many expressions of gratitude and kindness from his patients and that if at times he should lose faith in humanity these will help to restore it.

A third point which may have some effect on character is that the major part of eye work is meticulous and of an almost mathematical exactness which predisposes to clear thinking.

There are many other features of ophthalmic work which have been omitted in this short review, for example, the rush and hurry of a crowded out-patient department, the attempt to do good work with inadequate equipment, the realisation when teaching undergraduate students that ophthalmology is only a small branch of medicine and that all they want is the irreducible minimum of information. The first two may induce a feeling of frustration, but the last may beget some humility and a realisation that great though the field of ophthalmology may be, it is only part of the vast acreage of medicine, much of which we have not explored.

Such then is the environment in which we live and it seems to produce a kindly race of men with a wide knowledge of humanity, an ability to come to quick and wise decisions and a flair for accurate observation: That these and other qualities must have been present in some degree before engaging on ophthalmology is, of course, obvious, but that the practice of our profession encourages their growth seems a likely possibility.

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## ANGIOMATOSIS RETINAE, WITH REPORT OF PATHOLOGICAL EXAMINATION

BY

HUMPHREY NEAME

LONDON

IN view of (1) the rarity of the condition (2) the lack of reports of late results of treatment, and (3) the fact that the affected eye of the second case was excised and examined pathologically, the following two cases seem worthy of record. One, Ada C., was first examined in 1936, had both eyes affected and had varied treatment; the second, Violet H., was seen at Moorfields by several surgeons and a fundus drawing was made in 1939; the writer did not see her until November, 1946, when the affected eye was found to be painful, blind and glaucomatous, and was therefore excised.

Case 1. Ada C., aged 28 years, attended Moorfields Eye Hospital on February 8, 1936, complaining of blurring of the sight of the left eye, apparently of sudden onset. At that date the R.V. was 6/6 6/5 (partly), the L.V. 6/60. After dilatation of the pupils, examination of the right fundus through clear media showed a disc of healthy appearance, two very dilated vessels passing into the

inferior temporal region, and some hard white exudate like that of circinate retinopathy mostly between the vessels (see Fig. 1). In the 7 o'clock direction a rounded prominence of pinkish colour was visible in which the two large vessels were lost. The left eye, whose

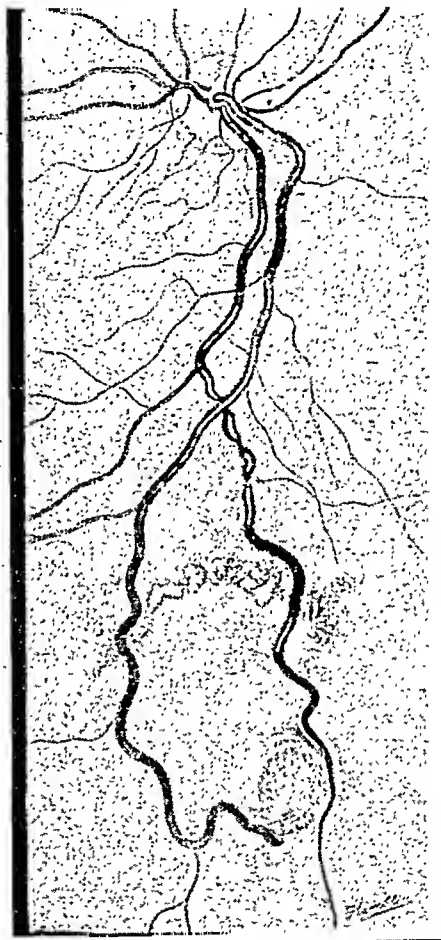


FIG. 1.

Ada C. Fundus drawing of the right eye, showing two dilated retinal vessels ending in a pinkish-coloured localised prominence. (The drawing has been rotated to save space. The angioma was in the 7 to 7.30 o'clock meridian).

media were also clear, showed two vessels of very large calibre passing from the optic disc in an upward direction, the larger being also very tortuous (see Fig. 2). A large area of hard white exudate occupied most of the area from the optic disc to the macula. Small retinal vessels lay anterior to the exudate. The enlarged

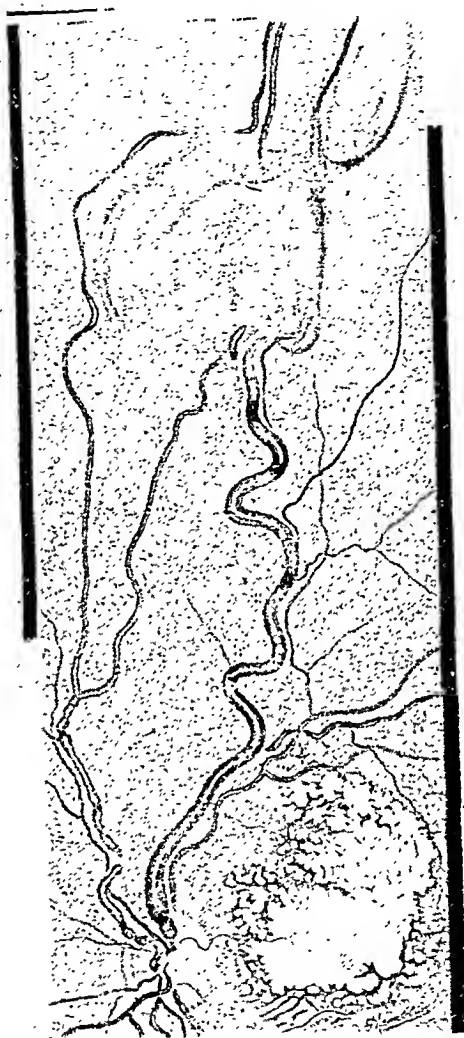


FIG. 2.

Ada C. Fundus drawing of the left eye, showing a similar appearance to that of fig. 1, but with two swellings in the upper periphery.

blood vessels led up to an oval pinkish prominence, in the 12 o'clock direction, fully 2 disc diameters in vertical dimension and rather less transversely. About 1 disc diameter further and slightly to the temporal side lay another similar prominence of smaller size. The retina in the region of the swellings and of the enlarged vessels had the appearance of being slightly detached.

By estimating disc diameters both from the disc to the swellings and from the swellings to the extreme periphery and assuming the

distance from disc margin to the limbus to be about 36.5 mm. in the two directions, it was calculated that the angioma in the right eye was 18.5 mm. from the limbus; in the left it was judged that the anterior limit of the smaller angioma was 23 mm. from the limbus.

*Treatment of the left eye.* Between February and June, 1936, the left eye was treated by electrolysis with a fine perforating needle 3 times. A galvanic current by the cathode was used at 2 milliamperes for 4 seconds to 4 milliamperes for 6 seconds, 10 to 12 punctures at each operation. A further application of electrolysis, 5 milliamperes for 10 seconds at each of 27 perforations, was made in June, 1937. Only at the second application of the 3 mm. fine needle did well-marked bubbles appear in the vitreous. At the end of this operation the whole of the angioma area was surrounded by the pale reaction of electrolysis. The 2 large retinal vessels were much reduced in calibre and little larger than normal retinal vessels.

As during succeeding months of 1937 the 2 angiomata in the left eye showed no signs of regression, treatment by the 1 gram radium bomb was applied. It is regretted that details of dosage cannot be traced. The patient, however, declares (1948) that 8 separate hours of treatment were given and further treatment stopped as loss of eyelashes took place in the lower eyelid. A total dosage of 14 hours had been planned. In the latter part of 1938 no definite improvement in the condition was detected. It was therefore decided to employ diathermy with a perforating needle.

On December 7, 1938, perforating diathermy was employed with 7 punctures. One of these coincided with the larger retinal vessel and one with the angioma. At the end of the operation the vitreous was very dark and vision barely perception of hand movements.

On January 2, 1939, the L.E. had vision still no more than perception of hand movements. The vitreous was very dark with a faint red reflex above.

*Treatment of the Right Eye.* On September 12, 1936, the right eye was treated by electrolysis under local anaesthesia aided by luminal and omnopon. A guide suture inserted at the limbus was carried across the cornea in the 6.30 meridian. A small puncture was made 22 mm. from the limbus in this line with a broad needle and a Foster Moore stud inserted. This showed ophthalmoscopically a white streak immediately posterior to the angioma and slightly temporal.

A galvanic current was then applied by means of a 3 mm. sharp needle on an insulated curved shaft, connected with the cathode. A current of 10 milliamperes was used at 12 points for 6 seconds.

each. The punctures were made as far as possible in a square area, at 1 to 1.5 mm. apart just anterior to the stud mark. At the end of the operation a mass of small bubbles was seen with the ophthalmoscope just posterior to the angioma and a wide area of pallor anterior to these. Finally 2 or 3 more punctures were made posterior to the stud in the hope of destroying the enlarged vessels.

On October 5, 1936, the vitreous was hazy but a large area of reaction was visible below with an outlying patch just below the macular area (from one of the latest applications).

On November 11, 1936, the R.V. with +2.25 sph.=6/12 the pupil being dilated. L.V. with +1.25=6/24. The angioma was visible in the right eye in an area of atrophy, but was estimated to be  $\frac{2}{3}$  disc diameter as compared with the estimate on September 10, 1936, of 1 d.d. across.

*Progress.* On May 18, 1939, two weeks after a blow on the forehead the patient noticed a cloud in front of the right eye. Several streaks of haemorrhage were visible on this date in the right vitreous. Dark streaks were still visible in the lower part of the vitreous cavity in March, 1940. The appearance of slight retinal detachment is noted below. Posterior cortical lens opacities are seen in the left eye, and a large retinal cyst in the lower periphery.

September 10, 1940. R.V. with lens=6/9, L.V. with lens less than 6/60. In the right, white proliferating tissue extends upwards from the most posterior point of electrolysis towards the fovea. Increasing retinal detachment below: L.E. anterior and posterior iridescent cortical lens opacities.

January 2, 1941. R.E. a delicate veil from the disc passes towards the macula. The lower retina is quite definitely detached. L. disc is barely visible owing to lens opacities.

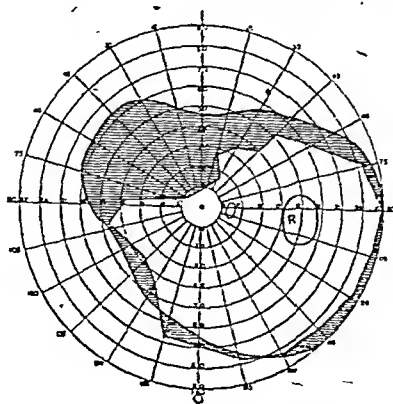


FIG. 3.

Ada C. Field of vision of right eye on October 22, 1941.  $\frac{1}{2}^\circ$  white object.

*Field of Vision.* Fields mapped by the perimeter before operation with  $1/4^\circ$  white object were full. The chart of October 22, 1941, with  $1/2^\circ$  white shows a representative right field of several charted after operation (Fig. 3). Bjerrum screen indicated encroachment towards the macula in the upper-nasal region to the  $8^\circ$  circle (4/2000 white object) on November 11, 1936.

On July 8, 1942, the loss had extended to the  $3^\circ$  circle (6/2000 white), and on January 20, 1948, to the fixation point (5/2000 white).

*Visual acuity.* November 11, 1936. R.V. (pupil dilated) with +2.25 sph. = 6/12, L.V. +1.25 = 6/24.

In 1943 on several occasions R.V. recorded as 6/9 with glass. In December, 1944, R.V. with glass = 6/18, and complaint made of recent dimness of sight. This was explained by vitreous floating opacities of a reddish colour.

November 6, 1946. R.V. with glass 6/12, 6/9 (4).  
+2.5

January 20, 1948. (H.N.) R.V.  $\frac{\quad}{+0.25 \text{ ax. } 90^\circ}$  = 6/24 6/18 (3).

L.V. perception of light with faulty projection.

## DISCUSSION

In view (1) of the tendency to bleed into the vitreous, as also observed by Foster Moore<sup>1</sup> after radon treatment, (2) of the very slow absorption of blood, and (3) the rucking of the retina which is evident between the disc and the lower part of the right macula and hence a fear of proliferating retinopathy, no further operative treatment to the right eye has been thought advisable.

In view of the slowly progressive loss of field with increasing retinal detachment below, it is intended to recommend diathermy puncture in 2 places in the hope that retinal cyst formation is the cause of detachment as occurred in the left eye.

Case 2. Violet H., married, aged 20 years. The patient attended Moorfields Eye Hospital early in October, 1946, complaining that the left eye had been aching on and off for two months.

*Previous History.* She had been to the London Hospital in 1935 where it was stated that she had a "birth-mark" at the back of the left eye.

In October, 1939, she first visited Moorfields. The writer first saw her in 1946. The recent in-patient notes record that she had been examined in 1939 by several members of the Honorary Staff and that the diagnosis of angiomas retinæ was made. (See Fig. 4, drawing of October 5, 1939.) She was admitted on November 5, 1946. The right eye was free from congestion, the

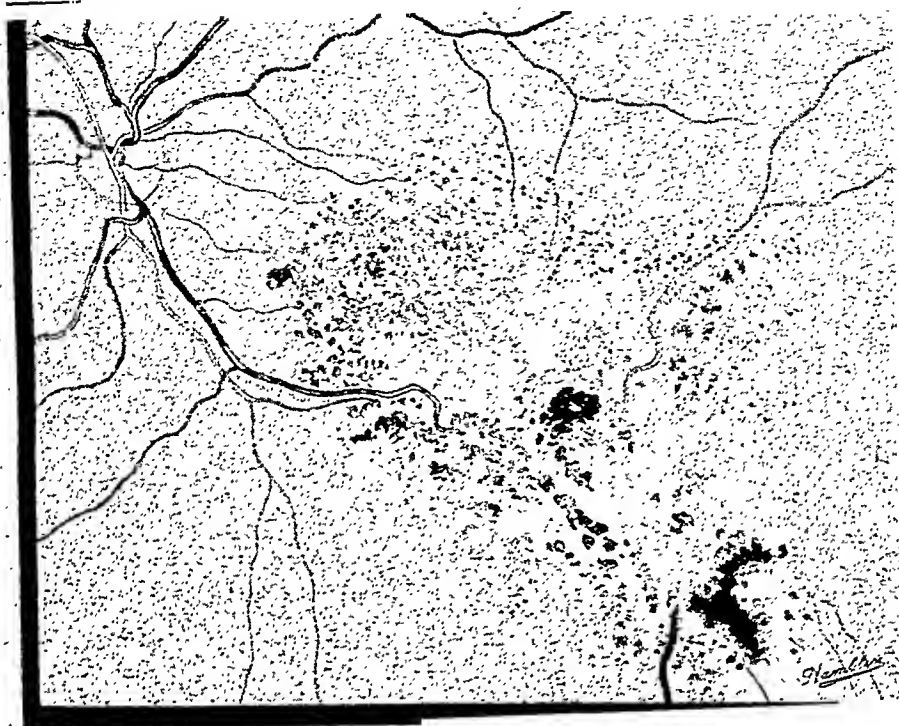


FIG. 4.

Violet H. Fundus drawing, left eye, October 5, 1939.

pupil circular and active, the media were clear and the fundus healthy. With  $-4.5$  dioptre sph.  $-0.5$  dioptre cyl.,  $180^\circ$ , vision was 6/6. Tension normal. The left eye was white, the cornea clear, and the pupil circular with no direct reaction to light and sluggish consensual reaction. No red reflex was obtained. A glistening mass was seen close behind the lens with numerous straight vessels coursing over it. The tension was much raised and there was no perception of light. To transillumination there was relative dullness below. The left eye was excised on November 6, 1946.

*Pathological examination.* The eye, fixed in Zenker's fluid, was embedded in celloidin and antero-posterior sections were cut. These were stained with haematoxylin and eosin.

**HISTOLOGICAL EXAMINATION.** *Path. No. R.L.O.H. 271/1946.*

Antero-posterior sections examined under Zeiss A. objective and No. 4 eye-piece showed a shallow anterior chamber whose angle was closed by apposition of the iris root to the cornea, completely



covering the region of the canal of Schlemm. There was atrophy of the iris and ciliary body with slight ectropion of the uvea. The lens was *in situ* and had retina closely in apposition to its posterior surface. The vitreous cavity was almost entirely obliterated by complete retinal detachment. A few small round cells and fibroblasts



FIG. 5.

Violet H. Microphotograph; magnification  $\times 35$ ; shows the most posterior part of the angiomatosis area of the detached retina. (Stained with haematoxylin and eosin). (a) indicates the largest blood-vessel in the group. Abundance of coarse vessels extend forwards in the cone-shaped mass of detached retina to an additional extent about equal to that shown in this photograph. (b) marks areas of haemorrhage in the retina.

were near the reflexion of the retina at the ora serrata. In the posterior folded up part of the detached retina were blood-vessels of large calibre with a number of smaller vessels lying among retinal elements whose layers cannot here be indentified. Partly surrounding several of the large vessels were masses of red corpuscles—haemorrhages, which may have been responsible for the recent subacute glaucoma (Fig. 5, microphoto 1). There was no trace of

any wall or boundary to indicate any localisation of the vascular growth. In fact an abundance of vessels extended in the section for about twice the expanse shown in Fig. 5, *i.e.*, some 6 millimetres in all. The subretinal space was partly occupied by some granular exudate containing numerous migrated rounded pigment cells with circular nuclei. The choroid vessels were full of red blood corpuscles and a fairly widespread round-celled infiltration affected the spaces between the vessels.

Examination under higher magnification showed the large blood-vessels to be very thin-walled, having little more than a single layer of endothelium. The layers of the retinal-structure could only be identified in the periphery, near the ora serrata. (Fig. 6, 7, 8.) No cystic changes were present in the sections examined.

The striking feature of this angioma is its diffuseness and complete absence of any definite boundary. Its extent in the sections shows that it had enlarged somewhat in the 7 years since the drawing was made. There is, however, no suggestion in the sections of malignancy. A comparison with the reproductions of the microphotographs of McDonald and Lippincott<sup>2</sup> shows a very close resemblance in structure. These writers, using glial stains, found only slight proliferation of the glial cells and concluded that this was secondary.



FIG. 6.

Violet H. Microphotograph; magnification  $\times 80$ . Portion of the section shown in Fig. 5. For (a) see Fig. 7; (b) haemorrhage.

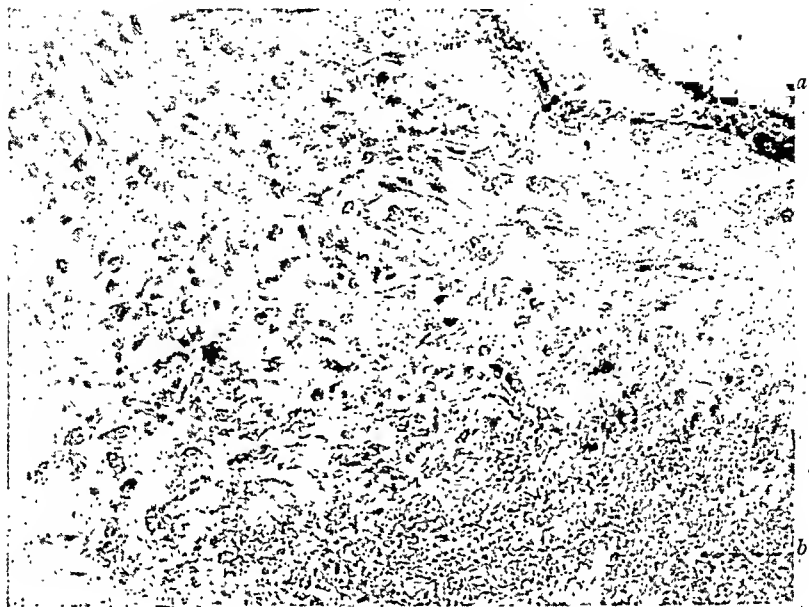


FIG. 7.

Violet H. Microphotograph;  $\times 260$ . The portion shown corresponds with (a) in Fig. 6; (b) marks the edge of a haemorrhagic area in the detached retina. The blood has shrunk away from the vessel-wall which shows a single layer of endothelium.

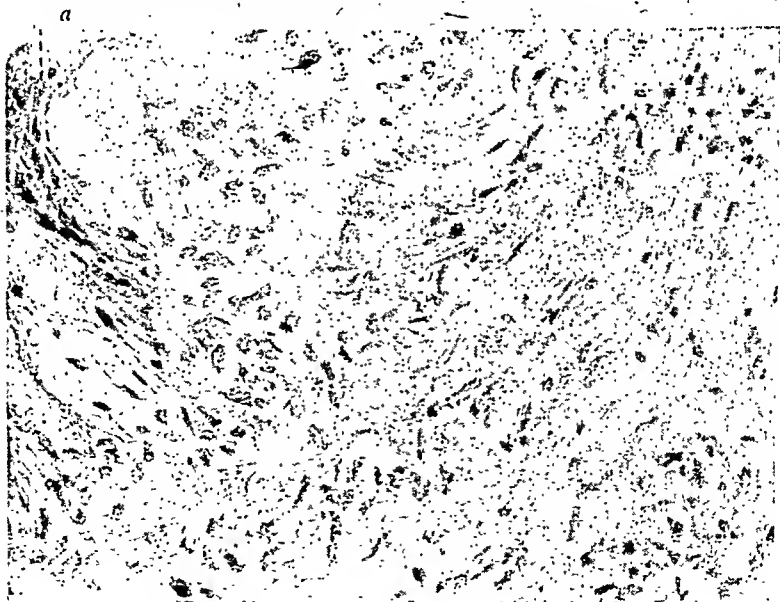


FIG. 8.

Violet H.  $\times 260$ . Showing cellular structure. (a) indicates a flattened blood-vessel which can be recognised opposite (c) in Fig. 5. (This vessel is at right-angles to its direction in Fig. 5. The lower border of Fig. 8 corresponds with the left-hand border of Fig. 5).



FIG. 9.

Nicolotte D. M. H. Whiting's case of bluish juxta-papillary angioma.  
October, 1945.



In addition to the above the writer has had the opportunity of examining two cases of a bluish-coloured angioma of venous appearance in addition to one reported by Nicoll and Moore<sup>3</sup>. The latter is also reproduced by, Elwyn<sup>4</sup>. The two cases were seen at Moorfields Eye Hospital in the clinics of Mr. M. H. Whiting and Mr. E. F. King to whom the writer is indebted for permission to refer to them. They were of exactly the same type as Nicoll and Moore's seen in 1934. In all three the bluish coloured prominence with a nodular surface was at, or overhanging the optic disc.

Case 3. Nicolette D. (Fig. 9). Aged 7 years. The patient was under Mr. Whiting at Moorfields Eye Hospital Out-Patient Department on September 26, 1945. R.V. 6/9. L.V. 6/6. A mulberry-like growth was seen to overhang the disc margin of the left eye. This had been noted by Mr. Joshua Keyms of Southampton who referred the case to Moorfields. The purplish-coloured mass was approximately circular and extended about half way over the disc. It was nodular, and definitely prominent. It appeared to be composed mainly of rather large veins (larger than the ordinary tributaries of the central vein).

A follow-up has recently been possible, thanks to the help of Mr. W. E. Heath of Rochester, in the first of two cases of capillary angioma treated by Moore<sup>1</sup> in 1934. The patient stated that her sight remained good for nearly 18 months after the radon treatment and then failed fairly rapidly owing to cataract.

TYPES OF ANGIOMATOSIS RETINAE. There seem to be two distinct clinical types; (1) the pale pinkish swelling or swellings connected with retinal vessels of fully 2 to 3 times the ordinary calibre. These are usually circumscribed and appear clinically to have an enclosing sheath or capsule. Rarely they appear to be without any capsule—see drawing of case 2 (Violet H., Fig. 4), as is confirmed in the histological sections. In these the prognosis is bad without treatment; (2) the bluish coloured venous-looking swelling of which three cases have been seen. One of these (Nicoll and Moore<sup>3</sup>) was excised and found to be non-malignant. These cases should be followed up to see if the swellings increase in size. Elwyn associates cases of other types of vascular anomaly with these; (1) Coats' disease with telangiectases, (2) Sturge-Weber disease, occasionally with dilated and tortuous retinal vessels, and (3) the extremely rare arterio-venous aneurysm of the retina.

TREATMENT. The pinkish capillary angioma associated with 2 vessels of large calibre, must be treated, as it leads inevitably to blindness. Radium, radon and X-rays have been used. In all of these cataract is to be expected as in Moore's case (radon<sup>1</sup>) sent by Heath, and the left eye of the author's case No. 1. In the

latter, to the left eye with two angiomas—one as much as 3 mm. across, with localised detachment already present—electrolysis applied on three separate occasions between February and June, 1936, did not suffice. Radium bomb was then employed in 1937. However, no notable change in the condition followed. Perforating diathermy was employed in December, 1938, as described, with vitreous haemorrhage. Cystic degeneration of the retina and cortical cataract were present 2 years later. The angioma in the right eye appeared to be swallowed up in fibrous tissue after electrolysis, but 2 bouts of vitreous haemorrhage have occurred since and a lowly progressive detachment of the retina. Foster Moore's second case treated by radon was not traceable. Of two cases treated by diathermy Weve's<sup>5</sup> had vision  $1/6$   $2\frac{1}{2}$  years after treatment of an angioma in the superior-temporal region above the macula, and retained practically a normal field. Michaelson's<sup>6</sup> case with an angioma not far to the temporal side of the macula and with a localised retinal detachment and a retinal hole, recovered to the extent of vision  $6/9$  with correction as compared with  $6/36$  before operation. This, however, was only  $3\frac{1}{2}$  months after operation and the angioma was only  $1/3$  disc diameter across.

The author favoured the use of the galvanic current as this has been a favourite method of treating spider-naevi in the skin of the face. It was hoped to puncture the angioma and apply sufficient current by the cathode to cause haemostasis. It is probable that with any but the smallest angiomas—*e.g.*, Michaelson's—this is still the ideal method. But the method of approach may perhaps be improved. It may be mentioned that the electrocautery is used by some dermatologists to destroy a spider naevus. As in the eye, however, only one shot can be made by this instrument and a bull's-eye must be scored, this technique is not feasible for the retina. It seems that, provided the angioma is not far in the periphery, a fine but rigid needle insulated nearly to its point might be used by the trans-scleral route while the fundus is under observation with the binocular ophthalmoscope through Goldmann's contact lens<sup>7</sup>. The latter used this method to apply diathermy to a macular hole in order to prevent detachment of the retina, as described by Foster<sup>8</sup>. In the second type of angioma, that composed of coarser bluish vessels, of which three cases have been mentioned, should definite evidence of increase in size be obtained, this may prove to be the best method of attack. The help of a physicist is needed in order to choose between the merits of galvanism or diathermy. In the 3 cases mentioned it would probably be desirable to use the kind of current whose destructive effect is the less extensive, so as to cause as little damage

to the optic nerve as possible. In any case there is a great probability that almost half the visual field would be lost. When the angioma is to the temporal side of the optic disc—macular vision would be destroyed. Better that, however, than loss of the eye.

Several unsolved problems exist in connexion with this condition :—

(1) Is there a tendency for new angiomata to form as occurred in one case mentioned and illustrated by Elwyn<sup>4</sup> ?

(2) Hard white exudates may be present early as in the right eye of case 1 described, long before any detachment was suspected. Are these due to haemorrhage in one whose retinal vessels are especially prone to leak ?

(3) Why does retinal detachment occur when there is apparently little subretinal exudate and no hole in the retina ?

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## VISUAL PROTECTION IN AERIAL WARFARE

BY

Air-Marshal P. C. LIVINGSTON

### INTRODUCTION.

IN order that men may bear weapons with success and fortitude in modern warfare, it is necessary that they be armed, not only with equipment suitable to the occasion, but with their minds prepared for such high adventure that the capacity for imagination is locked within the lower levels of consciousness. Throughout the World War, 1939/45, personal experience records no case where a member of aircrew became obsessed by a dread of blindness through enemy action. On the contrary, the destruction of sight appeared so little feared, that difficulty was experienced in persuading personnel of the air arm to take reasonable precautions against ocular injury. This negation of the thought of blindness



no doubt results from the acceptance of sight as a natural attribute, so much part of human structure that the catastrophe of its loss is beyond contemplation. Therefore, in the heat of action, it seems unthinkable that vision should be destroyed, leaving defenceless the combatant so afflicted. The very position of Man in the Universe signifies that the guiding hand which has led him safely through many hazards to his eventual goal, is dominated by a broadening mind reacting to impressions transmitted through the visual apparatus.

#### GENERAL CONSIDERATION.

In times of conflict it becomes necessary to introduce equipment aimed at the preservation of sight, without however creating a state of eye consciousness among those for whom the protective measures are intended. In lectures and demonstrations directed to this end, the audience should be regarded as containing a group of personnel who previously have given little thought to the risks to vision associated with aerial warfare, but are in fact strongly susceptible to suggestion. It becomes necessary therefore to exercise care in preserving the morale of aircrew personnel. Other difficulties occur peculiar to this branch of preventive medicine. No order exists which demands that aircrew personnel shall, under threat of penalty, adopt some special precaution designed for their safety. They may be called upon to carry a device with them on operational duty, but there is no guarantee as to its use. The problem becomes one of appeal to reason backed by sound argument. In this, as in so many other matters, the example set by Captains of aircraft becomes of particular significance. Aircrew are often hero worshippers. Frequently without a thought, they accept as indisputable the opinion of one well reputed for skill in combat. At times a situation so created may not be directed to the best interests of the Service, because some pilots of high achievement are individualists whose ideas do not conform to the recognised tactics of combat. It should fall to the lot of those whose duty it is to reduce wound incidence to offer their knowledge and experience in a manner which will create a proper understanding of the situation and of the elementary principles concerned. It is well appreciated that great individualists in War are not always the most suitable guides for a population so varied in background and psychological structure as that prevailing in aircrew. These features are stressed because they reveal a number of difficulties that may impede the use of apparatus constituting part of a campaign directed against traumatic blinding.

## EVENTS WHICH THREATEN BLINDNESS

Some operations of aerial warfare contain hazards common to combatant forces in general, others are peculiar to actions developing at altitude. Examples of the former are found in low level attack on enemy transport columns, railway systems or airfields. Here the defensive fire is commonly from machine guns, rifles and other light weapons.

High level operational flying draws fire from defensive weapons on the ground, such as light or heavy anti-aircraft guns and rockets, while in addition attack by machine gun or cannon fire may come from intercepting aircraft. Ocular injuries are found to occur from missiles intact, from fragments of these after explosion outside or inside the aircraft, or from shattered parts of the aircraft. Injuries of serious character are sustained through burns from fires started in fuel tanks or by the ignition of incendiary bombs carried within the aircraft. Fires following a crash on landing at base sometimes occur. A forced landing as a result of engine failure accounts for other forms of injury, as when the head strikes against projecting parts of the instrument panel, especially if the harness designed to restrain forward propulsion of the body happens to break.

Sudden structural failure of the air frame, in high speed manoeuvres, when for example portions of the engine cowling break away or a wing fractures, may terminate in severe facial injury involving the eyes. More rarely, wild fowl have been known to smash through the cabin structure and destroy vision.

The foreign bodies responsible for ocular injury sustained on flying duty may be metallic or non metallic. The metallic foreign bodies are more frequently non magnetic than magnetic. Therefore, the magnet in the extraction of these particles is of limited value. Experience tends to show that the eye is more tolerant of the presence of fragments of metallic alloys than was at first believed. An exception is copper.

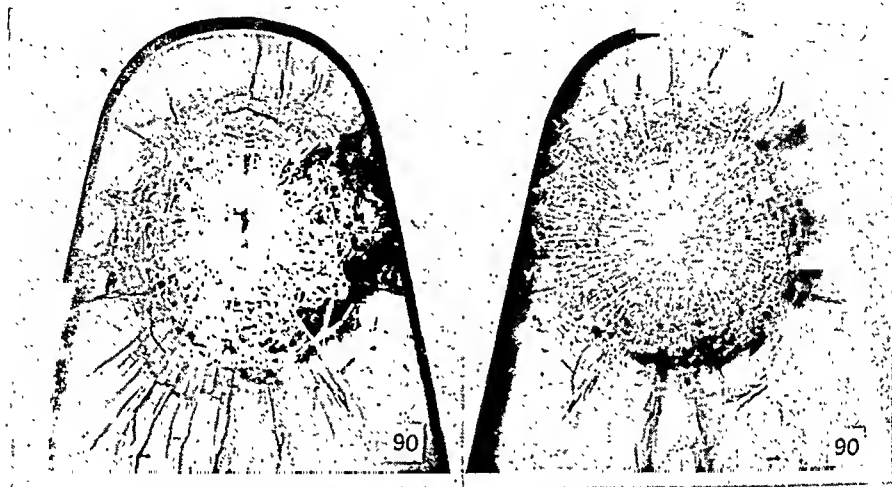
Perspex, one of the cellulose acetate group of materials used in aircraft cabin windows, is fortunately very well tolerated. It sometimes occurs that twenty or more tiny pieces of perspex become embedded in the cornea and remain without serious reaction occurring. The only unpleasant sequel is the abnormal dispersion when light strikes the surfaces of these translucent foreign bodies set at varied angles in the substance of the cornea.

## METHODS OF COMBATING OCULAR INJURY

These group themselves under three headings :

- (1) *Measures incorporated within the structure of the aircraft.*

(a) Bullet proof glass is constructed in layers united under pressure and held together by an adhesive substance. The glass plates so prepared attain a thickness of  $1\frac{1}{2}$ " or more. Welded steel or light alloy tubing comprise the supporting framework. Illustrations 1 and 2 show the effect produced upon the front screen of a fighter aircraft by the impact of a bullet at close range. Only a very few flakes have been detached on the side of the screen



— ILLUSTRATION 1.

Front surface of bullet proof glass windscreen, fighter aircraft showing effects produced by 0.303 armour piercing bullet at 200 yards.

ILLUSTRATION 2.

The same windscreen as (1), showing surface towards pilot. Note how few particles of glass have been shed from the mass of cracks.

next to the pilot. (2) This effect was produced by a .303 W. Mark I armour piercing bullet with a charge giving an equivalent range of 200 yards. A further example of the resistance of bullet proof glass is illustrated (3) in the case of a bomber aircraft. This sheet was situated behind the pilot on the starboard side. The photograph is taken looking aft. The attack was made by a Messerschmitt 210 whilst the Lancaster was on a mission to Frankfurt. The aircraft received 80 hits. Of these, two 792 mm. armour piercing bullets from dead astern and level, entered the rear end of the cockpit canopy on the starboard side shattering the 3" bullet proof slab. In this instance a cavity of approximately  $\frac{3}{8}$ " deep was made in the steel defence armour, positioned behind the pilot. A further illustration (4) provides an example of the devastating effect of close range night fighter fire upon the rear turret of a bomber aircraft. Protection in respect of the

gunner's turret is of necessity less complete than in the case of the pilot's cockpit, owing to the need to provide an observation post which permits a good area of search. There are a number of metal supports which offer secondary protection, but the fact that the turret is designed to rotate, exposes the gunner in a more vulnerable manner than is the case with other occupants of the aircraft. Furthermore, in order to obtain the best conditions of



ILLUSTRATION 3.

Bullet proof glass screen situated behind pilot of Lancaster III aircraft.  
Effect produced by 792 mm. armour piercing bullets.

visibility it became necessary to remove part of one of the perspex panels so as to provide an area through which search of the night sky could be made with full freedom.

(b) The use of armour is restricted by its weight. It affords excellent protection for the pilot. These plates are usually 12 mm. thick. They can resist a 20 mm. shell unless struck point on. Their value in visual protection is indirect. For example, they stop the flight of an explosive cannon shell, which unimpeded might come at a narrow angle from behind the pilot and exploding against the instrument panel, scatter at high velocity many particles of varied composition likely to endanger the eyes.

(2) *Equipment in the form of goggles, spectacles, visors and contact lenses worn by aircrew.* (a) All safety glass used in goggles is of the laminated form, that is, two sheets of glass connected by a flexible interlayer. It will be observed, in illustration (5) d to g, that goggle windows are composed of two surfaces meeting at an obtuse angle. This design was adopted in order to achieve great strength. It has been shown that curved safety

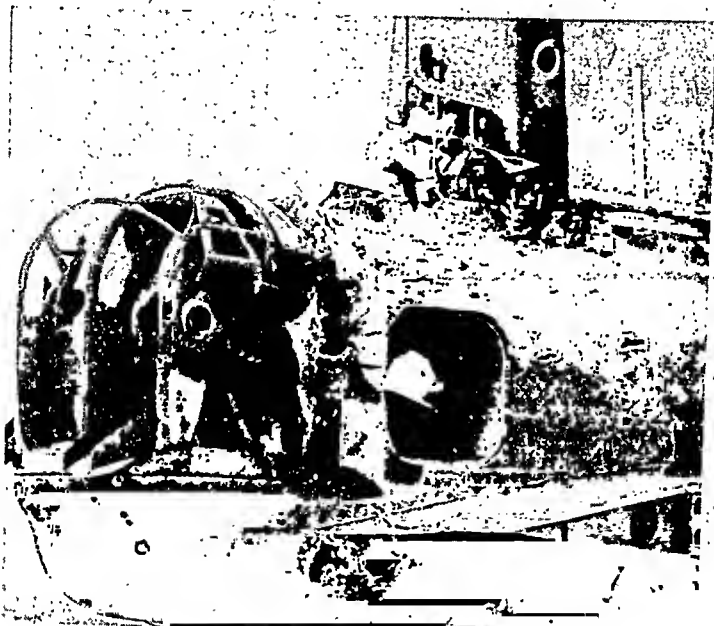


ILLUSTRATION 4.

Rear turret of Stirling aircraft after raid on Duisberg, April, 1943, showing severe damage to the rear gun turret and controls. This aircraft succeeded in reaching base.

glass as used in some types of goggle is not fully reliable. The principle of resistance to fracture is founded upon a precise union between surfaces. This union at the present time, can only be assured if the surfaces are flat. The specification under which goggle glass is passed as suitable is exacting, because the optical properties must be considered, as well as the safety factor. The test for splintering is made after accelerated ageing tests in which the glass is subjected to low temperature, hot moist air and ultra-violet light. For the splintering test, designed to eliminate glass which on fracture has a tendency to fly, the sample is held vertically and is struck centrally on one of its faces with

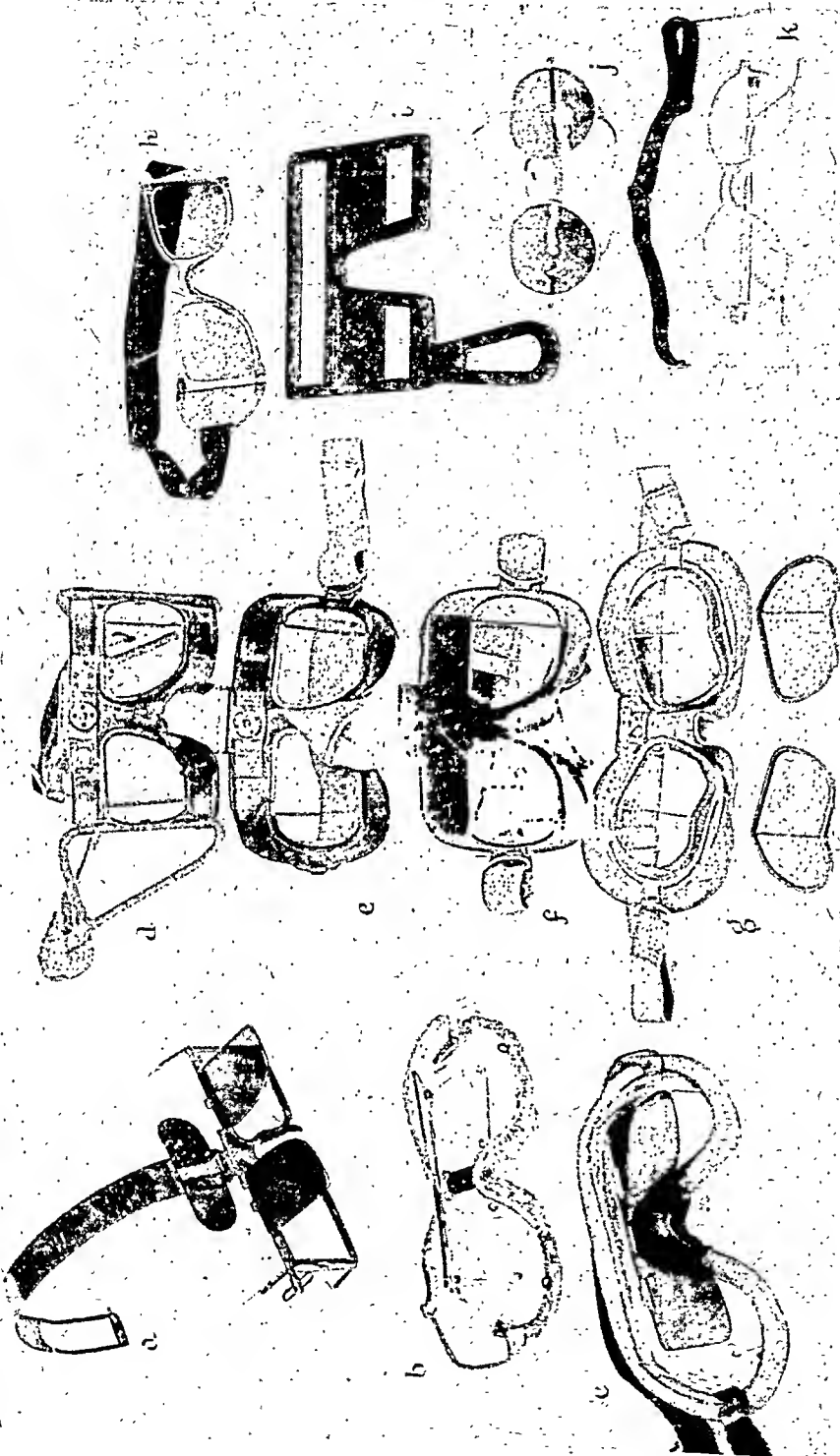


ILLUSTRATION 5.

Showing various designs of goggles, spectacles and visors resulting from the programme of development. The standard flying goggle is shown at *g*, with interchangeable windows untinted or tinted. The standard flying spectacle designed to receive corrected lenses at *k*, the present anti-glare glass spectacles at *j*.

a steel ball. Fragments which may be split from the other surface are collected on a lanoline treated body placed a short distance away. The sample is rejected if splinters are found adhering to the lanoline. Great difficulties were encountered during the development of safety goggles. The design even now is not settled. Flying goggles must be light and fit comfortably. They should not become fogged during the rapid changes in atmosphere frequently encountered at high altitude. The provision of a wide field of view is an essential requirement. It is important to provide protection against fire. Finally, the goggle must be of such shape as not to interfere with the fit of the flying helmet and oxygen mask. An idea of the work of development necessary in order to attain a satisfactory appliance is expressed in illustration (5) which from d to g shows some of the steps in design. The weight of goggle d was  $7\frac{3}{4}$  ounces, while that of goggle g was 4 ounces. Not only is a heavy goggle uncomfortable to wear on the ground; but it is also far more handicapping in certain manoeuvres in flight. During a sharp pull-out from a dive, the weight of a goggle may, for a few seconds, be increased by as much as fivefold and become displaced. As the weight factor is extremely important, an attempt was made to distribute pressures over the head from before backwards. The results shown at illustration (5), (a) proved unstable in wind. Masks such as (b) and (c) composed of synthetic material scratch too readily. Goggles of any form are not popular in aircraft with completely enclosed cabins, but are essential in some elementary training aircraft, and also in certain fighter aircraft, when the hood is moved to the open position for take off and landing. On occasions, a goggle has proved of value on abandoning the aircraft.

It has become necessary to provide safety spectacles of the type seen at (5), h, j and k. The spectacles are of two types, one intended for protection against glare (j), the other (k) for holding corrected lenses in the case of defective visual acuity. In order to provide a field of acute vision as wide as possible, it is necessary that the frames designed to hold correction fit close to the eyes. The lenses must be ground large. The measurements of the corrected safety lenses illustrated are  $44 \times 50$  mm. It is also necessary to provide a type of fitting which will maintain the spectacles in position in the presence of strong wind. The side pieces, therefore, are of metal closely applied to the sides of the head. An alternative fitting is provided which permits an elastic strap to be attached to the outside of the flying helmet.

(c) Visors made of synthetic material have been a source of experiment. Two factors, however, militate against favourable

results; namely the softness of the substance, thus causing a reduction in visual acuity owing to the rapid appearance of multiple scratches and the difficulty in obtaining the material suitably tinted to ward off sun glare direct or reflected. It is also to be observed that the synthetic substances of the cellulose acetate group permit the unimpeded passage of ultra-violet light in contra-distinction to the properties of glass. The advantages of visors of this character are that they are light and can readily be moulded to fit the curves of the head and the contours of equipment. Visors are illustrated at (5) b and c, with tinted shields attached.

(d) The employment of contact lenses is limited by the intolerance from ocular sensitivity, of about 60 per cent. of those who undergo preliminary trials with the shells which are employed in the first instance. They are of great value in the few instances in which tolerance exceeds seven hours. They are strong and very resistant to fracture owing to the elasticity of the orbital content against which they are forced in the event of a blow.

(3) *Methods adopted to increase visual perception.*—An indirect but highly important method of aiding visual protection is to build up a system of instruction with the idea of quickening visual perception, thus raising the speed of detection and recognition of aircraft by day or night. The greatest attention has been

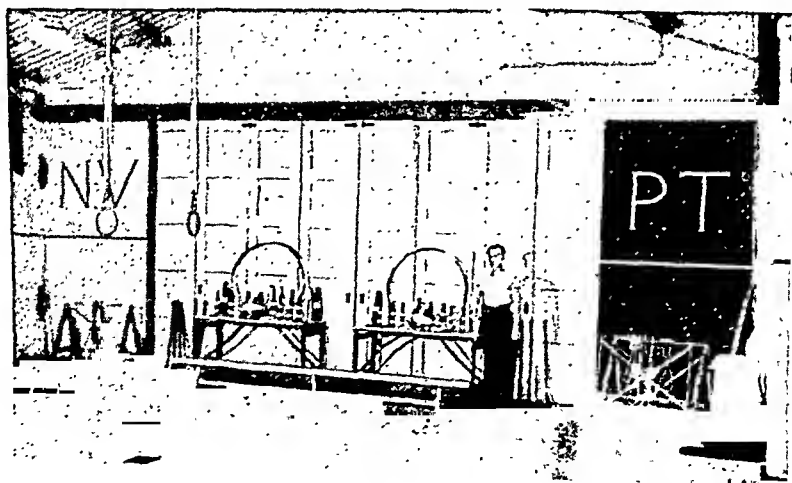


ILLUSTRATION 6.

A gymnasium used for night vision training. Note the black and white painted hoops and skittles, as well as the white trestle used in walking and balancing exercises under low illumination.



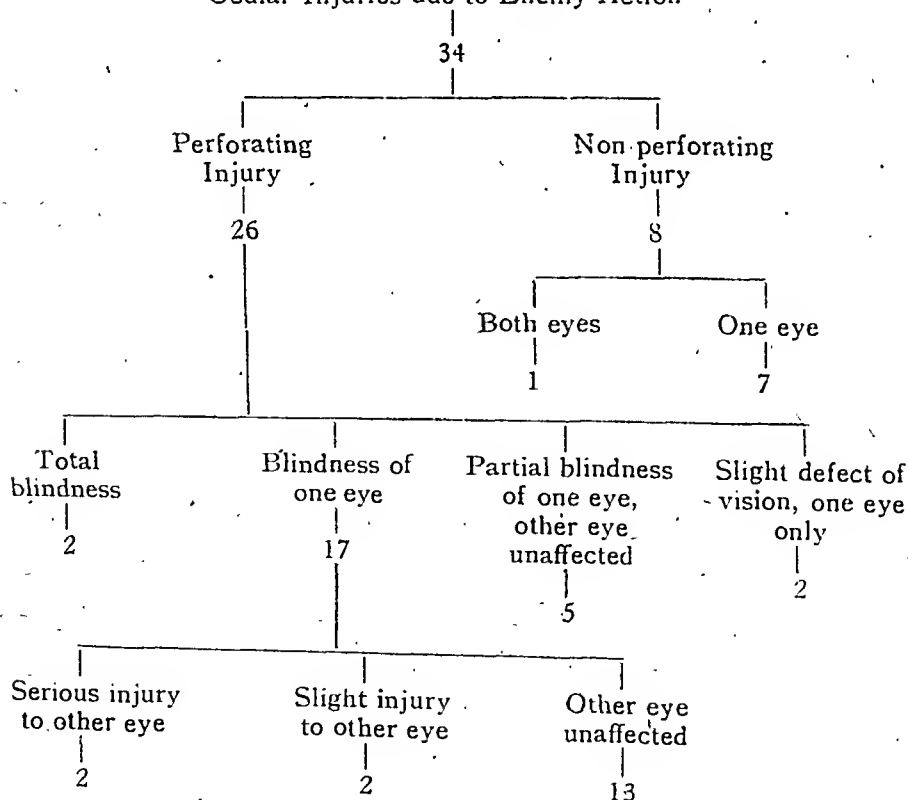
given to improving performance under conditions of low illumination. The problem is complicated and the benefit gained is based largely upon assumption without clear statistical proof. The basis of this form of training received strong approval at Royal Air Force Headquarters, especially in Bomber Command. Fighter Command developed the technique in respect of its night fighter pilots. The aircraft were later equipped with radar for establishing contact with the enemy outside visual range. It was nevertheless essential for the human eye to establish identification. Night vision training comprises lectures upon the general principles of scanning at night time, together with practice using various devices under conditions equivalent to moonlight and starlight. Demonstrations are provided which show the effects created by altering the position of the source of night illumination upon ground targets. Games are played under low illumination in the gymnasium as illustrated in (6) with the participators wearing light trapped safety goggles containing dark filters. After a few lessons the improvement in performance is often remarkable. In the case of night interceptor pilots special care is taken to assure a high standard of night visual capacity before flying training in this branch of aerial warfare is commenced.

### THE ASSESSMENT OF PROTECTIVE MEASURES

In estimating the full value of the measures which have been described, it is found very difficult to establish the position on a statistical footing. So many and varied are the situations encountered in War operations, that it is hard to discover sure ground from which the true value of visual protection can be calculated. For example, a number of personnel found it impossible to wear their goggles regardless of the wide field of vision provided and the eventual comfort attained, because they experienced a feeling of restriction, however good the optical qualities of the goggle glass. Much depends upon skill in the tactics of combat in the air which applies equally to both sides. Much of this skill is founded upon experience, with which goes a greater capacity for accurate and rapid visual perception. The element of fortune tends to exercise a strong influence upon the issue. It is, in truth, only possible to institute a search for various ways of protecting the eyes against injury, to employ every one that appears practical and likely to be appreciated, to spare no pains in explaining the value of these procedures, so that the greatest number of personnel will be encouraged to make use of them, and from this position to await the issue. One positive

approach in the campaign against blindness is the early elimination or treatment of those of doubtful visual capacity for day or night flying duties. At one time it was necessary to accept pilots with a visual acuity no better than 6/18 in both eyes correctable, however, at least to 6/6. To assist these personnel, over 12,000 goggles with correcting lenses were issued. The high standard of at least 6/6 in one eye and not worse than 6/9 in the other, was maintained for Air Gunners and Bomb Aimers. Over 200,000 tests for night visual capacity were carried out, with a rejection rate that rose to over 6 per cent. At the same time care was taken to observe personnel who were of borderline category in this respect, and have them sent to a special clinic if their performance in the air at night was adversely reported by the Captain of the aircraft. In this manner, in one year, over one hundred personnel were subjected to a careful examination in which the field of night vision was studied by means of self luminous targets, and eliminating action taken when field defects were discovered. Among such personnel were those who suffered from early retinal

### Ocular Injuries due to Enemy Action



disease, or from changes reflecting themselves in the scotopic visual field, as in diabetes.

### THE INCIDENCE OF BLINDNESS IN AIR CREW PERSONNEL IN FLIGHT

The total loss of sight of both eyes has occurred twice only in flying operations against the enemy. The after history of one case provides a fine example of the ability of youth to surmount this catastrophic event. Entering a University he studied law and obtained honours at the graduating examination. The policy which guides such cases into the care of the St. Dunstan's organisation is, without question, right. It is here alone that a full understanding of the psychology of blindness has been mastered.

The table, p. 699, provides an analysis of the ocular injuries from Royal Air Force records, confined to air engagements with the enemy.

### SUMMARY AND CONCLUSION

(1) The preservation of sight can be aided by the use of bullet proof glass screens and armour plates fitted within the structure of the aircraft.

(2) Further protection can be effected by equipping aircrew with flying goggles or spectacles fitted with safety glass windows which can be ground so as to provide correction in cases of refractive error, or by fitting contact lenses in certain cases in which the refractive error cannot be otherwise adequately treated. The eyes behind contact lenses can move over a wide range without loss of acuity.

(3) Visual training offers a valuable indirect method of protection by instructing personnel in careful scanning procedure, how to make the best use of rod vision under states of low illumination, and quickening the powers of recognition of the objects detected.

(4) The record of ocular injury sustained by personnel of the Royal Air Force in flying operations lends weight to the belief that a planned campaign against the hazard of loss of sight reaps its rewards.

GONIOTOMY FOR THE RELIEF OF  
CONGENITAL GLAUCOMA

BY

OTTO BARKAN

SAN FRANCISCO

CONGENITAL or infantile glaucoma (hydrophthalmos, buphthalmos), has been among the most hopeless of ocular conditions requiring surgery. In the past, rare cases in which sight was preserved by operation or by spontaneous arrest appear to be exceptions that prove the rule. Trephination has been unsuccessful and often disastrous, cyclodialysis ineffective. A few cases of normalisation of pressure over a period of years by iridencleisis have been reported.

In recent articles<sup>1,2</sup> observations on congenital glaucoma and the results obtained during the past ten years by goniotomy performed on 76 eyes presenting congenital glaucoma were published. In 66 of these pressure was normalised and vision maintained or restored. In ten the operation was unsuccessful.

Goniotomy is an operation for stripping or peeling embryonic tissue from the angle wall. If the cornea is clear the operation is performed under direct vision with the aid of a prismatic contact glass specially devised for this purpose. In this series the operation was performed under the contact glass on 20 eyes. On 56 eyes the operation was performed without the contact glass because of corneal cloudiness.\*

It is the purpose of the present article to discuss the diagnosis and cause of reduced vision in infantile glaucoma and to stress the urgent need of early adequate operation. The technique of goniotomy is described. Indications for the operation and its mode of action, which are essential to an understanding of its principle, are set forth.

The operation is exacting. It requires teamwork and demands meticulous attention to detail of technique in order to obtain a high incidence of good results and to avoid injury which may have tragic consequences. Experience with gonioscopy and acquaintance with the varying picture of congenital glaucoma are helpful.

## DIAGNOSIS

The early symptoms in congenital or infantile glaucoma are often of a congestive and irritative nature. In the present series out of 87 eyes, 70 showed congestive symptoms at the time of onset.

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\* The approach to the angle across the chamber was first introduced by de Vincentiis in 1892 and some successes were reported. The method later fell into disuse.

Congestive symptoms caused by increased pressure consist of:

1. Corneal cloudiness, minor or extreme.
2. Hyperaemia of the bulbar conjunctiva, slight to moderate.
3. Photophobia, which may be extreme.
4. Epiphora.
5. Blepharospasm.

In 30 eyes cloudy cornea was present at birth. In 35 eyes the onset of congestive symptoms appeared between the first and fourth



FIG. 1.

(Pre-operative).—P.O'Q., aged 5 months, first seen July 25, 1944. Cloudy cornea developed six days before. Patient showed slight photophobia and tearing since birth. Pupils are in miosis due to three instillations of 5 per cent. solution of prostigmine every three hours.



FIG. 2.

(Post-operative).—P.O'Q., aged 2½ years. From August 9, 1944, to October 2, 1945, four goniotomies were performed on each eye: The last operation on the right eye was nine months ago, and on the left eye eighteen months ago. Note clear cornea, normal-appearing eyes and complete absence of symptoms. Tension (McLean) March 17, 1946, was 34 mm. in the right eye and 34 mm. in the left eye without use of miotics. Refraction was -2.00 sphere in each eye. Ophthalmoscopic examination showed normal appearance of heads of optic nerves.

months. In 11 eyes the onset was between the fourth and ninth months. Some increase of pressure and enlargement of the eyeballs was present before congestive symptoms appeared, since these

children are often described as having had especially beautiful (i.e., large) eyes. This appearance in otherwise normal looking eyes should arouse suspicion. Usually, however, the onset of congestive symptoms is the feature which calls attention



FIG. 3.

(Pre-operative).—T.C., aged 11 months, first seen July 10, 1942. Two months previously, on May 11, 1942, cornea of left eye became cloudy overnight. There were photophobia and tearing. The eye could be opened with difficulty; the bulbus was enlarged.

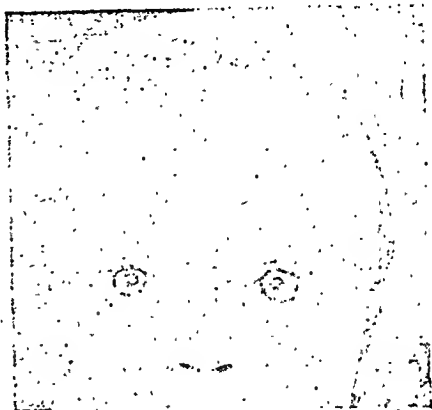


FIG. 4.

(Post-operative).—T.C., aged 14 months, three months after goniotomy was performed on the left eye, on August 21, 1942. Note clear cornea. The left eye is slightly enlarged, but is otherwise normal in appearance. On May 25, 1944, twenty-one months after the operation, tension (McLean) was 29 mm. in the right eye and 28 mm. in the left eye without use of miotics. Refraction was as follows: right eye, -1.00 sph. -1.00 cyl. axis 180°; left eye -3.50 sphere. Gonioscopy of the left eye showed stripping of angle in one-third of its circumference. Ophthalmoscopic examination showed wide shallow excavation of the head of the optic nerve of the left eye but no atrophy.

to the condition; the onset is often rapid and may be even sudden. Such was the case in six infants in this series in whom cloudiness of the cornea was discovered by the mother when the infant was taken up in the morning; the eyes had been clear the previous night. In one case the cloudiness was discovered when the infant was taken up from its afternoon nap.

The cloudiness of the cornea is often associated with photophobia, which may be so intense that the eyes cannot be opened except in the dark. For this reason it was impossible to obtain pre-operative photographs in many cases. Fig. 1 illustrates moderate cloudiness of the cornea. Fig. 2 shows the same patient



FIG. 5.

(Pre-operative).—J.V., aged 6 years. Since birth left eye was slightly larger and cloudy; there was some tearing. When first seen May 10, 1943, tension in right eye was normal, and in left eye was  $-1$  to  $-2$ . Photograph shows patient avoiding light. There is some tearing.



FIG. 6.

(Post-operative).—J.V., aged 7 years. Goniotomy was performed on left eye May 12, 1943. Photograph shows patient one year after operation. Note clear cornea, absence of photophobia and normal appearance. Patient was last seen July 2, 1946, three years, two months after operation; excellent condition had been maintained; tension in right eye was 31, in left eye 33 (McLean), without miotics; media were clear; ophthalmoscopic examination showed wide shallow excavation of head of optic nerve not extending to the rim; colour of disc was good. Vision without correction, in right eye, is 0.8; in left eye, 0.4. With correction, vision in left eye is  $-0.50$  sph.  $-0.75$  cyl. axis  $90^\circ$ , = 0.6 and J.—2.

post-operatively. Figs. 3 and 5 illustrate pre-operative congestive signs of minor degree which permitted of photography. Figs. 4 and 6 show the same patients post-operatively. In the case of T.M., aged 11 months, the eyes were of normal appearance until the age of 6 months when, following whooping cough and pneumonia, the mother noticed cloudy corneae. From then on the child was

extremely photophobic. It spent its life playing at night in a dark room and sleeping during the day. When brought for examination it kept its head buried in its mother's bosom. A glimpse of the eyes could be obtained only by separation of the lids by force because of the intense blepharospasm. Ten days after goniotomy the corneae were clear and photophobia almost absent. Fig. 7



FIG. 7.-

(*Post-operative*).—T.M., aged 11 months, first seen July 14, 1943. After whooping cough and pneumonia at the age of 6 months both corneae became cloudy and photophobia was extreme, so that the eyes could not be opened in daylight. Goniotomy was performed six months after the onset of symptoms, on the right eye on May 17 and on the left eye on May 20, 1943. Nine days after the operation the corneae were clear, eyes were open and patient tolerated light well. Eyes were normal in appearance, except for slightly increased size. There was no sign of corneal opacity, but retinoscopy showed slight irregular corneal astigmatism. There was myopia of approximately  $-2.00$  sphere. On September 27, 1944 (sixteen months after the operation), tension (McLean) was 29 mm. in the right eye and 20 mm. in the left eye without miotics. In June, 1946 (three years after the operation) a letter from Texas reported patient's condition to be excellent to date.

shows this patient 16 months post-operatively. The corneae are clear; vision is excellent.

The corneal cloudiness and lack of lustre which is characteristic of the early stage was shown by staining with fluorescein to be due chiefly to a disturbance of the epithelium. It appears that it is largely this disturbance, consisting of roughening of the corneal



epithelium, which is the cause of the irritative symptoms and photophobia.

A physician who first sees the child with these congestive symptoms is apt to make a diagnosis of conjunctivitis, blepharitis or keratitis. He is not prone to think of glaucoma because the term "buphthalmos" is associated in his mind only with enlargement of the eyeball. The resulting delay in arriving at the correct diagnosis and instituting proper and adequate treatment may be tragic, for by the time the eyeball is strikingly enlarged the patient is usually well on his way to semi or total blindness. Therefore, in every case in infants in which irritative phenomena or corneal cloudiness are present, even though the bulbus does not appear enlarged, glaucoma must be suspected and intra-ocular pressure tested with a tonometer.

Tension should always be measured under ether anaesthesia which must be sufficient to assure complete relaxation at the moment of measurement. Other general anaesthetic agents have proved unsatisfactory. It has been found that tension may vary 10 to 15 mm. of mercury, depending on the depth of anaesthesia, and only when the patient was completely relaxed was the tension constant. Cases have been observed in which increased tension due to insufficient anaesthesia led to an incorrect diagnosis of congenital glaucoma. In the present series of cases in which the pressure was elevated, prostigmine 5 per cent. was instilled in the eyes every three hours and goniotomy performed as soon as possible.

In cases in which the cornea is sufficiently transparent one finds on careful gonioscopic examination characteristic evidence of congenital glaucoma in the chamber angle.

#### CAUSE OF REDUCED VISION IN INFANTILE GLAUCOMA

Anderson<sup>3</sup> has pointed out that the cause of reduced vision in infantile glaucoma is usually regarded as being optic atrophy and one or more disorders in addition. In the present series atrophy of the optic nerve and others of these disorders were not the original cause, but were the result of progressive enlargement of the eyeballs and of tissue degeneration associated with the late, advanced stage of the disease. The primary cause of reduced vision in most cases in the series was a disturbance of the cornea. This disturbance begins with corneal cloudiness (oedema?). It appears to coincide with the onset of increased intra-ocular pressure. Allowed to persist it is followed by permanent scarring of the cornea with associated irregular astigmatism and ensuing amblyopia of greater or less degree. In those cases in which corneal cloudiness was relieved within a few days after onset acute vision developed.

## EFFECTS OF HYPERTENSION

(a) *Corneal cloudiness* is the main characteristic of the congestive phase of the early stage and at this stage is completely reversible surgically and occasionally by administration of miotics. The cloudiness usually occupies the central area. In severe cases it may cover the entire cornea, leaving only a strip adjoining the limbus clear. Fluorescein stains such corneae. Exposure to air, such as occurs when the blinking reflex is prevented while the patient is under general anaesthesia, increases the cloudiness and staining within a few seconds; if the lids are kept closed for a few minutes these decrease. That the corneal lesion is at least partially dependent on exposure is confirmed by its characteristic localization in the palpebral fissure zone. Abrasion of the epithelium in these cases shows a clear parenchyma in the denuded area. Another form of cloudiness appears in some cases to be due to an optical derangement of the corneal fibres. This cloudiness is evanescent. It can be produced by pressing on the bulb; on relieving the pressure the cloudiness disappears.

The roughened epithelium appears to be the cause of the irritative symptoms which in turn are aggravated by exposure to air and by light. These irritative symptoms promptly disappeared following normalization of pressure, coincident with the simultaneous restoration of corneal lustre and epithelial integrity. Clinically the child's comfort closely paralleled the epithelial integrity. Patients presenting high intra-ocular pressure and good corneal lustre are usually comfortable and show no trace of photophobia or other irritative signs. Patients presenting lower pressure and poor corneal lustre display irritative symptoms. The tolerance of the cornea to increased pressure manifests great individual variation. In some cases in which the tension is 50 McLean the cornea may remain clear and irritative symptoms be absent during the course of many months; in others the development of the same degree of tension may immediately produce marked cloudiness and irritability.

Cloudiness of the corneae at this early age sometimes is associated with nystagmoid movements. In two cases these were relieved by clearing of the cornea. To illustrate: J. McL., born with cloudy corneae, presented marked nystagmoid movements when first seen at the age of five months. Three weeks after normalization of pressure in both eyes by goniotomy, these had greatly decreased. They disappeared almost entirely in the course of the next several months. In the case of J. H., aged three months when first examined, corneal cloudiness had developed two weeks previously. During the interval of 15 days which elapsed between

operation on the two eyes nystagmoid movements made their appearance. Two weeks after operation on the second eye when pressure was normalized and the corneae were clear, these disappeared.

Cloudiness of the cornea requires quick relief (1) because of the rapidity with which it interferes with the development of vision, and (2) because the longer it exists the denser and more extensive will be the ensuing permanent scar. The present series shows that corneal cloudiness can be relieved and that in most cases formation of a permanent corneal opacity and development of amblyopia can be prevented in great measure by early diagnosis and prompt operation.

(b) The cloudiness becomes a permanent scar. This "late" milky opacification develops from the original reversible congestive cloudiness of the cornea when the latter has lasted sufficiently long to cause permanent damage to the corneal parenchyma. The prolonged distention *per se* may also be a factor in its formation, or both factors may be operating concurrently. This type is reversible in part only: It involves chiefly the anterior layers of the corneal parenchyma. The epithelium shows normal to fair lustre and does not stain to fluorescein if the eye is in a non-congestive phase. Certain of these cases show relative absence of congestive symptoms because compensation has taken place. Pressure may actually be less than in the early stage, perhaps partially due to thinning of the tunics of the distended eye and possibly also to increased permeability of the occluding persistent meshwork in the angle resulting from stretching. The latter may be the mechanism, as has been suggested, which accounts for some of the rare cases of spontaneous arrest.

(c) *Amblyopia*. It is essential for the physician to keep in mind that a cloudy cornea during the first year of life, unless promptly relieved, retards the proper development of central vision at a most critical time. These cases illustrate the susceptibility of the development of visual function to normal entry of light through the refractive media in the first year of life. They stress the urgency of prompt and adequate surgical interference. They also show the need for diligent continued observation after pressure has been normalized, in order to detect beginning strabismus which could rapidly induce amblyopia unless proper treatment with complete occlusion of the fellow eye is instituted.

(d) *Glaucomatous atrophy of the optic nerve* was the exception in this series. It occurred only in those few cases in which normalization of pressure was unduly delayed. In the case of B.O.S. (Fig. 9), patient did not come to operation until the age of  $4\frac{1}{2}$  years. The left eye had been lost due to atrophy following a



FIG. 8.

(*Post-operative*).—H.B., aged 7 months, when first seen on June 28, 1939. Three months previously the cornea of the left eye had become cloudy. Tension in the right eye was 20 mm. and in the left 90 mm. (McLean). Goniotomy was performed on the left eye on June 29, 1939. Drops of 5 per cent. solution of prostigmine were instilled every three hours in both eyes. On August 7, 1939, the tension (McLean) during ether anaesthesia was 50 mm. in the right eye and 31 mm. in the left. The cornea of the right eye was cloudy. Goniotomy was performed on the right eye. Three days after the operation the cornea of the right eye was clear. On November 27, 1939, three months after the operation the tension (McLean) in the right eye was 22 mm. and in the left was 22 mm. without miotics. On August 12, 1942, when the patient was aged 3 years 9 months, vision of the right eye without correction was 0.5 and of the left was 1/200. When the patient was last seen, on June 12, 1946, when he was aged 7 years and 7 months, his condition was the same, and the tension was normal. The right eye was emmetropic, the left eye myopic -3.50 sphere. The reduced vision of the left eye appeared to be due to amblyopia which developed during a transitory period of strabismus. Binocular fixation was present.



FIG. 9.

(*Post-operative*).—B.O'S., aged 4 years, first seen July 20, 1945. The left eye had been lost through trephine six months before. The cornea of the right eye was clear; tension (McLean) with miotics was 70 mm. Ophthalmoscopic examination showed glaucomatous excavation of the nerve head to the rim with slight pallor temporally. Vision was excellent, and visual fields were grossly normal. Goniotomy on the right eye with the contact glass was performed on October 12, 1945. Three months afterward tension (McLean) in the right eye was 26 mm. without miotics.

trephine operation performed at the age of four years. The right eye carried a pressure of 50 mm. Hg, McLean while under the influence of miotics. It showed marked glaucomatous cupping of the nerve-head to the rim. Because the cornea was clear excellent central vision had developed. This has been maintained since normalization of pressure by means of goniotomy performed one year ago. It is interesting to note, incidentally, that the excavation of the nerve-head almost disappeared following normalization of pressure. In the case of B.P., who was first seen when 5 weeks old, repeated goniotomy and other operations were unsuccessful on one eye for two years; by the time pressure had become normalized optic atrophy had occurred. In the case of L.L., aged 3 years, bilateral trephination with total iridectomy had been performed at the age of 8 months without permanently reducing tension. Cyclo-diathermy also failed permanently to reduce tension. At the age of 3 years goniotomy was performed; pressure was normalized in both eyes, congestive symptoms which had persisted until this time were completely relieved and the corneae cleared considerably. Moderate reduction of vision was found to be due in part to faint corneal scarring with irregular astigmatism and in part to glaucomatous atrophy which had occurred as a result of the protracted period of time during which the pressure remained elevated.

Ruptures or tears of Descemet's membrane, which are prominently referred to in the literature describing the pathological anatomy of "buphthalmos," were absent in this series of infantile glaucoma. It appears that tears of Descemet's membrane in infantile glaucoma do not occur before marked distension and degenerative changes have taken place. These conditions did not exist at the time goniotomy was performed in this series, which probably accounts for the absence of tears. If this observation is correct, rupture of Descemet's membrane plays no rôle in diagnosis at the time when diagnosis is of therapeutic importance.

#### MODE OF ACTION OF GONIOTOMY

In congenital glaucoma the angle presents a characteristic gonioscopic appearance which shows little individual variation. Other anomalies such as gross anterior adhesions were present in only 2 out of 77 eyes examined by the writer. The characteristic condition appears to consist of an abnormal insertion of the iris, by means of adventitious mesoblastic tissue into the angle wall anterior to its place of normal insertion.\* Gonioscopic examination

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\* Gonioscopy of normal eyes of infants indicates that the chamber angle does not assume adult appearance until after the age of several months indicating that the uveal meshwork continues to regress after birth. This appearance can in most cases be distinguished from the pathological persistence of uveal tissue which is present in congenital glaucoma.

with hand slit-lamp and binocular microscope held in the hand reveals that the iris continues in a horizontal plane until it reaches the posterior surface of the cornea. This is in contrast to dipping backwards of the iris as seen in the adult, thus forming a sinus or the so-called chamber angle. The point of attachment corresponds to the position of the anterior border ring of Schwalbe. The area of transition from the anterior surface of the iris to the posterior surface of the cornea consists of a gelatinous looking semi-transparent substance. This area may be so narrow that it barely constitutes a line. It may be wider, in which case the beam of light shows the tissue to be in a plane anterior or axial to the true angle



FIG. 10.

Drawing shows post-operative microgonioscopic appearance at the point of transition between the area on the right in which the angle has been stripped and the neighbouring untouched region.

wall the presence of which can in some cases be discerned in a deeper plane. Delicate arborescences of uveal meshwork which cross the angle can be seen resting on the semi-transparent substance which fills the angle behind them. From this finding and from the flare of the beam of the slit-lamp traversing it, it is evident that the angle is not an optically empty space. This fact becomes especially evident post-operatively at the point of transition between the area in which the angle has been stripped and the neighbouring untouched region (Fig. 10). The gonioscopic appearance corresponds to that which would be expected from a study of histological sections of eyes affected with congenital glaucoma enucleated in the early stages. Post-operative gonioscopy in the successful cases revealed that the procedure had been effective in stripping the persistent embryonic tissue that obstructed the filtration angle over

an area from one-fourth to one-third of its circumference. Figure 10 shows a case in which stripping successfully normalized pressure. Analysis of this series of cases suggests that stripping of this amount of the angle is sufficient and is the *sine qua non* of successful normalization of pressure. It also suggests that stripping of only a part of the circumference is adequate to permit the pressure regulating mechanism to assert itself and permanently to maintain normal tension and function. Since this effect has been observed in individual cases as long as 10 years after goniotomy, and since cases of recurrence of increased pressure have been the exception, it appears that the effect is permanent.

In all bilateral cases in this series and in most monocular cases, judging from results obtained by stripping the angle and by pre-operative and post-operative gonioscopic examination, the initial increased pressure appeared to be the result of obstruction of the angle due to arrested regression of the uveal meshwork. Since removal of the persistent embryonic tissue resulted in normalization of pressure, it must be assumed that Schlemm's canal was present. There was no sign that either internal cyclodialysis or external filtration had taken place in any of these cases. One may conclude, therefore, that the mode of action of goniotomy consists in restoring access of aqueous to Schlemm's canal by removing obstructing tissue.

In one case there was direct gonioscopic evidence of the presence of Schlemm's canal in that portion of the angle from which the obstructing tissue had been removed. This consisted of a pink band which was seen to lie external to the trabeculum in the position of Schlemm's canal. In the adult this pink band has been shown by Kronfeld to be produced by blood in Schlemm's canal<sup>4</sup>. The presence of Schlemm's canal is suggested by the post-operative gonioscopic findings in the aforementioned successful cases. It is confirmed by the analysis of anatomical examination of 84 specimens taken from unoperated eyes, as reported by Anderson<sup>5</sup>. He found that Schlemm's canal was present in 75 per cent. of the earliest specimens. No sign of it was found in more than half the specimens taken from children over 2½ years of age. He suggests that the canal becomes closed in the later stages as the result of distension of the eyeball and of increased intra-ocular pressure. The evidence obtained from these specimens thus confirms the rationale based on gonioscopic examination of the effectiveness of stripping the angle in early congenital glaucoma.

#### URGENT NEED FOR EARLY OPERATION

The mode of action of the operation as explained in the foregoing shows the importance of early diagnosis for a successful

outcome of operation, and explains why the chances of establishing outflow with this operation may be expected to diminish with the duration of the condition. It is essential to operate early before prolonged distension of the eyeball has caused obliteration of Schlemm's canal. Other important reasons for early diagnosis and prompt operation are :

1. Restoration of vision by means of clearing the cornea. Corneal cloudiness is largely reversible in the early stages, progressively less so in later stages.
2. Prevention of amblyopia due to prolonged obstruction of vision by cloudiness of the cornea.
3. Prevention of permanent scar formation developing from corneal cloudiness.
4. Prevention of injury to the optic nerve caused by prolonged pressure.

In general, it is important to prevent progressive enlargement of the eyeball before distension has produced permanent changes and to encourage development of normal anatomy and of physiological function during the period of growth.

## RESULTS

The results of goniotomy\* in congenital glaucoma are summarized in the following tabulation :—

TABLE I

### *Goniotomy in Congenital Glaucoma*

Number of infants and children ...	...	...	...	...	51
Eyes operated on by goniotomy ...	...	...	...	...	76
Successful (pressure normalized; vision maintained or restored) ...	...	...	...	...	66
Unsuccessful ...	...	...	...	...	10
Eyes on which goniotomy was not applicable ...	...	...	...	...	11

It has been my custom to prescribe miotics three times daily for two months after surgery. The result of the operation was considered successful when intra-ocular pressure never rose higher

\* Goniotomy in infants and in adults is two distinct operations which differ in rationale, technique and effectivity. In infants the operation, which has been developed to a relatively satisfactory conclusion, consists of removing occluding foetal meshwork from the angle. In adults, in whom it has not yet shown an adequate degree of consistent efficacy to recommend its employment except in the occasional case, its objective is to incise the angle wall, that is the trabeculum proper. For this reason it is suggested that the term goniotomy be applied only to the operation performed on infants, and goniotrabeculotomy or trabeculotomy to the procedure carried out on adults.



than 35 mm. of mercury with the McLean or 21 mm. with the Schiötz tonometer three months after operation, no miotics having been used during the two weeks preceding measurement of the pressure.

Among the successful cases the time elapsed since the date of operation varied from six months to ten years. There were recurrences in two eyes, mentioned in the next paragraph. The oldest case (two eyes) was operated on ten years ago; 5 eyes seven years ago; 8 eyes six years ago; 21 eyes from four to six years ago; 11 eyes from two to four years ago; 9 eyes from one to two years ago and 10 eyes from three to twelve months ago.

The recurrence of increased pressure which took place in two eyes was relieved by a second goniotomy in both instances. In F.W. pressure increased in the left eye eight years after operation. In J. McL., pressure increased in the left eye four years after operation. Gonioscopic examination showed that the stripping of the angle had been insufficient.

Repeated operations were necessary in 22 eyes before pressure was permanently normalized. One operation sufficed in each of 45 eyes. In some cases, for example that of P.O'Q. (Fig. 1), goniotomy was performed four times on each eye before permanent normalization was attained. The ultimate result was excellent. I believe it is better to err on the conservative side and partially strip the angle with safety on repeated occasions than to attempt to do an extensive stripping at one operation at the cost of greater hazard. Cases which required repeated operations before permanent normalization was attained are not listed as recurrences.

The operation was performed under the contact glass on 20 eyes. *All of these were successful. Repeated operation is the exception when operating under the contact glass.* In 56 eyes the operation was performed without the contact glass because of corneal cloudiness. On 18 of these repeated operation was necessary.

In 8 eyes which had been ineffectively trephined goniotomy normalized tension.

#### ADVANTAGES, DISADVANTAGES AND HAZARDS

Striking among the results of goniotomy are absence of cosmetic disfigurement and preservation of a round central freely reacting pupil.

A disadvantageous feature of the operation without the glass is the need to repeat the operation in one-third of the cases in order to obtain permanent normalization of tension.

Hazards of the operation are excessive haemorrhage or iridodiolysis if the root of the iris is incised. Vision was lost in two

eyes early in this series as the result of excessive haemorrhage. Recently one eye in a congestive neglected case of a  $2\frac{1}{2}$  year old child was lost as the result of a massive intra-ocular haemorrhage which occurred on the sixth post-operative day. Infection, as in any other intra-ocular operation, is a possible complication but was not encountered in this series. A severe reaction occurred in one case which could be considered an infective iritis. As always the eyes had been operated on different days, in this instance after an interval of three weeks. The condition cleared after 18 days leaving in one eye a small central opacity of the anterior capsule; in the other an anterior adhesion produced eccentricity of the pupil. Tension was normalized and it is evident that useful vision is developing. Sympathetic ophthalmia has occurred in no case up to the present time.

### INDICATIONS

Goniotomy is indicated in all bilateral and unilateral cases of congenital glaucoma in which increased pressure is the result of obstruction of the angle by persistent embryonic tissue, provided that Schlemm's canal has not been obliterated by prolonged distension of the bulbus. This includes the majority of cases of congenital glaucoma in the early stages. Generally speaking, the earlier it is applied after onset of symptoms the more effective is the operation in maintaining and restoring vision. Results may be dramatic when the bulbus is in the early congestive phase associated with cloudiness of the cornea. In these cases the urgent need for early diagnosis and prompt adequate operation can hardly be over-emphasized. There are cases, however, which run a chronic course during which the corneae remain clear, the optic nerve undergoes little damage and the bulbus is only moderately enlarged after a long period of time. Good central vision is maintained in them. Since the corneae are clear goniotomy can be performed under direct vision with the aid of the glass, and may be effective several years after the onset of symptoms. Excellent results were obtained in some of these cases at 4 and 6 years of age with corneal diameters of 14 mm.

### CONTRA-INDICATIONS

Goniotomy is contra-indicated in older children with enlarged eyes, that is, in eyes in the advanced stage which have had a congestive history with consequent corneal scarring and cloudiness and a corneal diameter of 15 mm. or more. In these enlarged "buphthalmic" bulbi the danger of haemorrhage is greatly

increased because of dilated vessels and collateral circulation which has become established. Haemorrhage is absorbed more slowly, no doubt due to degenerative condition of the eyes and to their changed circulation. Schlemm's canal may be obliterated as a result of the distension.

When permanent obliteration of the canal has taken place and when repeated goniotomies have proved ineffective, iridencleisis or cyclodiathermy may be tried.

Some rare unilateral cases of congenital glaucoma appear to be the result of other kinds of anomalies, such as an aberrant reflection of the iris stroma to an insertion at the anterior border ring. The extremely rare cases of narrow angle (angle or iris-block) glaucoma<sup>6,7</sup> in small children do not come within the scope of this article since goniotomy is not applicable to them.

### TECHNIQUE

There are two major procedures of goniotomy: if the cornea is clear goniotomy is performed by direct vision under a prismatic contact glass; if the cornea is cloudy it is done without the glass. The general considerations which the procedures have in common will be treated first.

### GENERAL CONSIDERATIONS

*Pre-operative measures.* Paediatric examination including X-ray of the chest for enlarged thymus is performed in all cases. In the case of infants, the usual diet is maintained up to 6 hours pre-operatively; sugar solution is forced up to 4 hours pre-operatively to avoid dehydration with associated hyperpyrexia. In order that surgery may not be delayed and since ether may have to be given several times in the course of the following weeks, every effort should be made to prevent the infant from catching cold. Miotics, preferably prostigmine 5 per cent., are continued usually every 3 hours while the patient is awake until  $1\frac{1}{2}$  hours before the time of operation. One extra drop is instilled three times at intervals of half hours before operation in the eye to be operated upon. If circumstances permit one drop of sulmefrin is instilled t.i.d. for several days pre-operatively.

*Anaesthesia.* In view of the delicacy of the operation as applied to infants, which may be only a few days or weeks old, anaesthesia is an important factor. A preliminary injection of atropine is given 45 minutes pre-operatively. Ether is administered through a small airway (intraparyngeal insufflation). A generous supply of oxygen should be assured at all times. While the patient is being

prepared the lids must be kept closed with moist pledgets but without pressure, since the cornea in congenital glaucoma is extremely susceptible to exposure and to pressure. For the same reason the heat generated by operating room lamps should be avoided. Anaesthesia must be sufficient at the moment of operation in order that there be no movement of the patient. In children over six months of age a small dose of paraldehyde is administered rectally 45 minutes pre-operatively. Post-operative agitation which may follow ether anaesthesia is not harmful since there is only a small obliquely placed puncture wound which does not permit egress of ocular contents. Before the patient is draped pressure is taken with a tonometer, the base of which has been sterilized. The corneal diameters are measured, and the condition of the cornea and size of the pupils noted. Sometimes the decision of which eye to operate upon can be made only at this time.\* Then the position of the patient, operator, assistant, anaesthetist and instrument table is arranged accordingly.

*Position of Patient.* The infant is placed on a circumcision board : for the right eye on the centre of the operating table ; for the left eye with the head end of the board protruding obliquely off the table. For operation under the glass the eye should be 47 inches above the floor to permit a convenient position for an operator 5 feet 10 inches in height. For goniotomy without the glass the patient's eye should be 46 inches or less above the floor in order that the operator may look vertically down upon it. A pillow or towels are placed under the head bringing it into a horizontal plane. The anaesthetist maintains the head in position during the operation.

*Position of Operator and his Assistants.* The operator stands on the side of the eye to be operated on : for the right eye at 11 o'clock ; for the left eye, at 4 o'clock. The illuminator holding a hammer lamp must be high enough, standing on a platform if necessary, to obtain a good view of the field of operation. He stands on the same side and to the right of the surgeon for the operation with the glass, on the opposite side for operation without the glass. The assistant fixates the bulbus with two Gifford forceps with lock, standing at 3 o'clock for the right eye and behind the head for the left eye. The anaesthetist is on the side opposite the operator, for the right eye at 5 o'clock in order not to interfere with the assistant who is standing at 3 o'clock.

*Magnification.* The operator uses a +2.50 sphere hanger over his correction. He wears a binocular head loupe +5.00 sphere

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\* In cases in which the decision has already been made the taking of the tension is dispensed with as a preliminary procedure in order to reduce the time of anaesthesia.

(Hess head loupe) which he uses only in case the anterior chamber is deepened through a corneal puncture made with a discission knife. He does not use it for the goniotomy.

*Illumination.* The room is in semi-darkness. One lamp situated at some distance from the table and directed away from it is in readiness for general utility purposes. The field of operation is

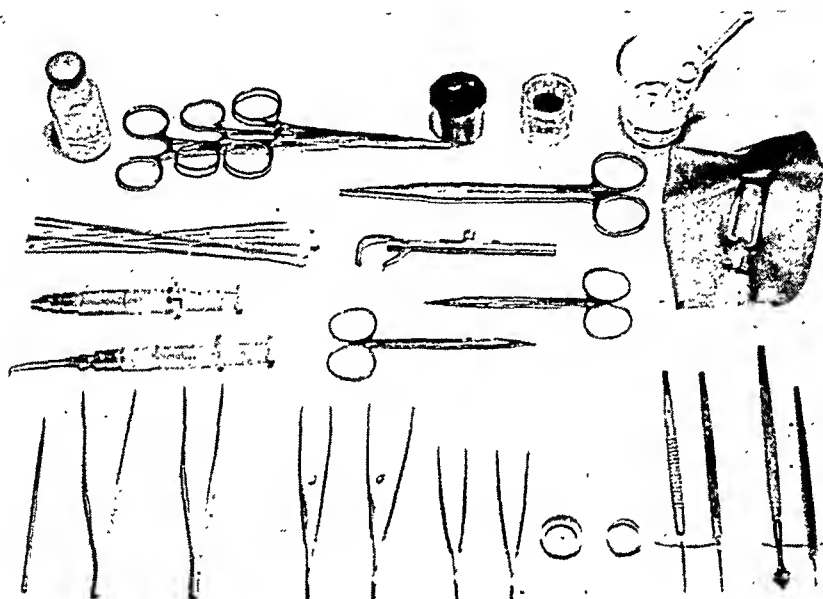


FIG. 11

Usual set-up tray for Goniotomy. Ampoule of physiological saline. Haemostats, mosquito. Dappen glass containing tincture of iodine. Dappen glass containing solution fluorescein, 1 per cent. Medicine glass containing physiological saline and glass rod. Speculum with rubber dam. Applicators. Mayo scissors. Luer-Lok syringe, 2 c.c. with # 30 needle, containing physiological saline solution.—Caliper. Stevens' scissors. Lacrimal dilator. Splinter forceps. Gifford's forceps with lock. Bishop-Harman's forceps. Surgical contact glass (small and large). Goniotomy knives. Keratome. Discission knife, narrow.

illuminated by a hammer lamp\* which is made of light plastic and is air cooled. It is used in both procedures but manipulation differs respectively. The illuminator must be familiar with and trained in the procedure. The technique of illumination is especially important in goniotomy by direct vision under the glass and must be carefully rehearsed before the operation.

*Instrument tables.* Small and large instrument tables are on the side of the eye to be operated upon (Fig. 11).

\* This lamp was demonstrated at the meeting of the A.M.A. in San Francisco, July 4, 1946. A description of it is in publication.

*Preparation of Patient.* Lashes are clipped (with Stevens' scissors and ointment, -wiped off with cotton spindle after each clip). The face is prepared and the eye irrigated in the usual manner. After the patient is draped a face mask, which should be of moistened gauze in order to be easily moulded to the region, is applied.

### GONIOTOMY UNDER THE CONTACT GLASS

Once the glass has been applied, time is the essence of goniotomy. A complete check, therefore, is made beforehand in order to assure that everything is in readiness and in position on the instrument table. The speculum is passed through two holes made in a piece of rubber dam 6 inches square. The height of the assistant and of the illuminator is checked. Either or both may require a platform to stand on. The lids are kept closed throughout the preparation. A few minims of adrenalin 1:1000 are injected with a  $\frac{1}{2}$ -30 needle and 1.5 c.c. Luer syringe into the outer canthus; after one minute a canthotomy is performed with straight Mayo scissors. The quartz surgical contact glass which has been cold sterilized is dried and placed on gauze in a small bowl on the instrument table. The knives (2 goniotomy and 2 discission knives) are now placed on the table, points toward the operator.

The operator stands at 11 o'clock for the right eye and at 4 o'clock for the left eye. The platform upon which the illuminator is about to stand is already in position to the operator's right. The instrument table and surgical nurse are also to the right of the operator. The speculum is now inserted and the rubber dam trimmed especially on the nasal side. On the temporal side the dam covers the lids, preventing contact of the knife with them and relieving the operator's mind of this important detail. The cornea is moistened when necessary with physiological saline solution applied by means of a glass rod. The eye is fixated by the assistant 2 to 3 mm. posterior to the corneo-scleral border at 12 and 6 o'clock by means of two Gifford forceps with spring lock. He must be mindful not to touch the lock lest it spring open during the operation. The head and eye are rotated away from the surgeon who applies the contact glass in the usual manner by injecting physiological saline solution between it and cornea through a Becton, Dickinson curved gold canula and 1.5 c.c. Luer syringe.

When operating on the right eye (Fig. 12) the fixator's right hand holds the forceps at 12 o'clock, the left at 6. The left hand must be in such a position that it does not obstruct the view of the illuminator as he moves counter-clockwise. When operating on the left eye, the right hand is at 6 o'clock and the left at 12.

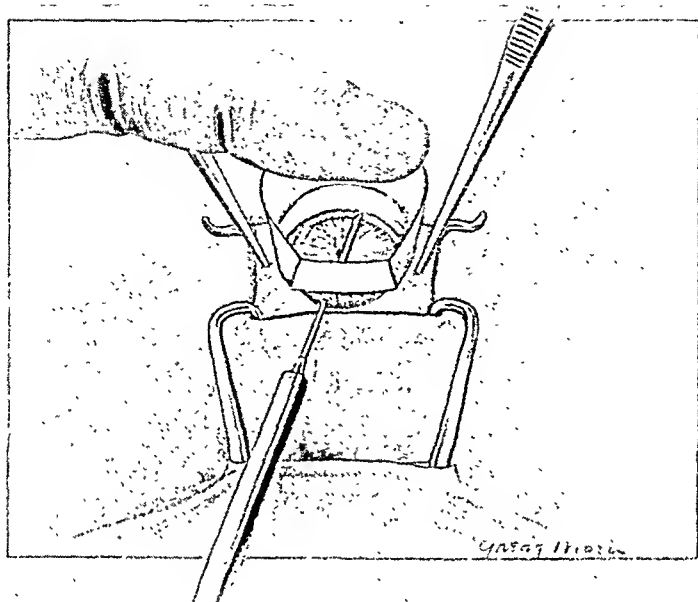


FIG. 12

Drawing shows goniotomy or stripping of the angle under the glass. The root of the iris retracts behind the blade, leaving a white wake behind it which is the wall of the angle.

Regardless of the side under operation, the fixator, unless tall, should stand on a platform in order to assure visibility of the eye throughout the procedure and to prevent the tendency arising from poor visibility to retract or dimple with the forceps. The surgeon supports the glass with the index finger of his left hand. Two indentations on top of the glass prevent the finger from slipping. The fixator abducts the eye slightly in order to expose a strip of the temporal portion of the cornea 2 or 3 mm. wide where the puncture is about to be made. By abduction the eye can be made to offer resistance to the glass when this is pressed more firmly against it by the operator's finger at the moment of puncture, thus preventing ingress of air at this critical moment. The operator applies the end of a cotton applicator previously dipped in tincture of iodine at the intended site of puncture. The goniotomy knife is then passed to him by the instrument nurse. She retracts the instrument table and the illuminator assumes his position on the platform immediately to the operator's right.

The illuminator stands on the platform sufficiently far removed from the surgeon to provide room for him to sway counter-

clockwise during the progress of the incision. The illuminator must stand with feet well apart in order to be able to sway in unison with the counter-clockwise movement of the surgeon without having to take a step. He maintains the lamp in contact with the temple of the surgeon, at the same time looking down the top of the shaft of the lamp, so that he may have the same view of the angle and of the blade of the knife as the surgeon. The heads should maintain contact. Perfect synchronization of heads and light is necessary; they must move as one unit. A light on a head band did not give as good results as the technique described.

The eye first having been rotated 2 hours counter-clockwise puncture is made in the right eye at 10 o'clock, in the left at 4 o'clock, 1 mm. anterior or axial to the corneo-scleral border and oblique so that the corneal wound is valve or trapdoor-like. At the moment of puncture, extra pressure is exerted by the operator's index finger on the glass in order to prevent ingress of air. Pressure must be exerted in the direction of the optic axis as tilting of the glass permits entrance of air. For the same reason dimpling of the sclera with the fixator's forceps must be avoided. The operator guides the knife across the pupil to the opposite side. In traversing the chamber the knife must always cross the optic axis. When the knife crosses the optic axis the diameter of the arc described after the opposite angle is engaged will be greater than the diameter of the circumference of the limbus. Therefore, the point of the knife remains engaged. When the knife does not cross the optic axis, the contrary holds true. In describing a smaller arc than that of the limbus, the point of the knife becomes disengaged and too small an incision is made. Moreover, the extra movement of advancing the knife necessary to maintain contact with the angle wall is prone to result in picking up iris tissue near the root with consequent iridodialysis and haemorrhage. The blade is inserted just anterior to the root of the iris and is moved counter-clockwise in this plane as long as visibility permits. This usually amounts to several millimetres or from one-fourth to one-third the circumference. During this excursion of the blade, the shaft is rotated around its axis in a clockwise direction to encourage a stripping action and to prevent the blade from moving posteriorly out of the intended plane into the dangerous region of the ciliary body. During stripping under the glass, the root of the iris is seen to retract behind the blade, leaving a white wake behind it which is the wall of the angle. In some cases this has the appearance of a cut piece of parchment paper that drops backward as the incision proceeds. Stripping should be under complete control and placed immediately above the root of the iris, care being exercised to avoid blood vessels at the iris root which in some cases



are clearly visible. There may be a slight sensation of grating as the blade proceeds; the fixator may recognize the need of exerting slight resistance. Since picking up the root of the iris causes haemorrhage it is advisable to start well anterior to the root and to strip or peel off the insertion of the iris from above. When stripping has been completed the knife is quickly removed, without loss of aqueous in most cases, care being taken to avoid enlarging the puncture wound in the cornea by slight pressure against the back of the blade during its removal. The contact glass and fixating forceps are withdrawn. After a few seconds a slight oozing of blood of venous colour appears in the anterior chamber along the line of stripping; this is absorbed within a few hours. If after removal of the knife the pupil should be eccentric, the cornea is tapped near the puncture with a spatula or the tip of a lacrimal dilator is inserted to prevent adhesion of iris to the inner wound lip.

The speculum is removed and the canthotomy closed with catgut. Eserine ointment 1 per cent, and sulphathiazole ointment 10 per cent. are inserted into the conjunctival sac. Binocular pads are applied, that over the operated eye being covered by a metal shield. The child is placed in bed on the operated side in order that any blood may settle on the opposite side of the chamber. Arm cuffs are applied. In older children, restrainers may be necessary. Elixir phenobarbital dram 1 may be indicated. After 24 hours it has been customary in bilateral glaucoma to instil prostigmine 5 per cent. in the unoperated eye and after 48 hours in the operated eye; thereafter drops are continued three times a day in both eyes. Only one eye is operated on at a time.

If the different steps of the procedure have been reviewed pre-operatively there should be no loss of time at operation so that once the glass is applied goniotomy is quickly completed.

If goniotomy under the glass is not feasible, the operation is performed without the glass. Operating under the contact glass is desirable whenever possible. In the past various procedures (use of glycerin, hypertonic salt solution, retrobulbar injection of adrenalin 1:1000 *inter al.*) have been tried without success with a view of clearing a cornea which has become cloudy during pre-operative manoeuvres, application of forceps and glass. Letting off a small amount of aqueous through a valve-like corneal puncture made with a Graefe knife was also tried. It cleared the cornea but did not permit of adequate operation under the glass because of complicating circumstances. *Recently a preliminary operative abrasion of the epithelium prior to application of the contact glass has enabled operation under the glass in cases in which it has heretofore been impossible.*

## GONIOTOMY WITHOUT THE CONTACT GLASS

The preparatory measures already outlined for goniotomy under the glass are carried out. The precautions mentioned under general consideration are observed. The height of the eye should be such that the operator looks vertically down upon it. Illumination is provided by the hammer lamp carried on the end of a rod so that the light falls as nearly vertically from above as possible. The illuminator stands opposite the surgeon, for the right eye at 4 o'clock and for the left eye at 10 o'clock. The rubber dam on the nasal side must be trimmed well back to avoid casting a shadow on the field of operation. The bulbous is fixated with two forceps held by the assistant, in the same manner as for the operation under the glass. The forceps should be vertical to the sclera and must include episcleral fibres in order to permit of resistance or counter-pressure on the part of the fixator during stripping. Additional fixation by the operator with a Bishop Harman forceps held in his left hand is helpful. If the assistant is not sufficiently experienced with this operation, it is best to divide the fixation between him and the surgeon. In this case the surgeon fixates with the Gifford forceps with lock in his left hand at 12 o'clock on the right eye and at 6 o'clock on the left, while the assistant fixates with his left hand at 6 o'clock on the right eye and at 12 o'clock on the left.

Canthotomy is indicated in most cases. In small infants, on whom the operation is especially delicate, the head is rotated toward the surgeon and the eye slightly abducted in order to bring the nasal limbus into a frontal plane to the surgeon's line of regard. In the case of a greatly enlarged eye this lateral movement is limited because the temporal limbus disappears as the result of even slight abduction. The surgeon applies Bishop Harman forceps at the contra-lateral limbus, helping to fixate and guide the rotation from there.

The puncture in the cornea is made as already described, being sure that it is oblique (valve-like) in order to encourage retention and reformation of the anterior chamber. It is made on the right eye at 10 o'clock, the eye having first been rotated counter-clockwise 2 hours. The blade of the knife crosses the pupil and disappears behind the limbus on the opposite side in a plane just anterior to that of the iris. As it engages the angle wall and starts its excursion in a counter-clockwise direction slight resistance is felt. Its tip can be seen through the sclera from the outside. Seen through the cornea, the knife appears 0.5 mm. farther anterior than it is in actuality. This appearance must not influence the surgeon to guide his knife farther posteriorly. A posterior position

of the blade is the greatest hazard of the operation. It is better to err on the conservative side by maintaining a more anterior plane at the risk of not stripping the angle. The operation can always be repeated. Rotation of the knife clockwise around its own axis helps to prevent it from being guided or from slipping to a posterior position. Stripping the angle wall is usually associated with a feeling of slight resistance and of grating if the blade is not too sharp. The absence of this feeling is an indication that the blade is too far posterior and must be avoided. If indicated the knife may be reversed and the stripping repeated in the opposite direction.

If upon re-examination later this goniotomy proves to have been insufficient, another can be performed on an adjoining part of the angle after suitable rotation of the eyeball. It has been possible in some cases, as shown by post-operative gonioscopy, to strip the angle over almost one-half its circumference at one sitting. Picking up the root of the iris and haemorrhage are the only serious complications to be guarded against. It has been found that removal of blood from the anterior chamber by paracentesis and irrigation cannot be adequately accomplished in infants. It is better to be obliged to repeat the operation than to provoke a major haemorrhage by too posterior position of the blade or by attempting too extensive stripping. If the stripping has been properly placed a little blood of venous colour begins to ooze from several points along the line of stripping a few seconds after removal of the knife. If the head is rotated to the opposite side, the blood coalesces to a thin sheet in the region of the pupil and is seen to stop. If the blood is more arterial in colour, is more extensive and follows immediately upon the incision, it is an indication that the latter has been placed more posterior than is desirable. Blood may fill one-half the chamber; it is usually absorbed within 24 to 48 hours.

The canthotomy wound is sutured, medications given and dressing applied as already outlined in the procedure under the glass.

*Notes on Stripping of the Angle.* In congenital glaucoma, there is an area of from 2 to 3 hours in the circumference of the angle opposite the point of puncture in which it is easiest to make an adequate stripping. Since the position of the puncture is limited on the right eye by the brow and on the left by the cheek bone, a point is chosen as far as possible in a clockwise direction—for instance, on the right eye at 10.30 o'clock in order to strike the opposite nasal angle as far clockwise as possible, *i.e.*, 4.30 o'clock. When the blade has reached 2.30 o'clock it has covered the area in which stripping can be done under optimum conditions and with least hazard. Post-operative gonioscopy shows that it is often possible

to strip a more extensive area, up to 4 hours or more by the clock. Since this cannot be done consistently and since it is associated with greater hazard of haemorrhage, it is well to consider allocating the area of the first stripping in such a way that another area of the angle as yet untouched can be stripped on a second occasion. For this purpose it is advisable in both procedures, with and without the glass, to start with the eye rotated 2 hours in a counter-clockwise direction. Thus for operation on the right eye the bulbus is rotated in a counter-clockwise direction so as to bring the area between 6 and 3 of the nasal angle within operative reach. The assistant maintains the bulbus in this position and resists, if necessary, the traction of the blade while it strips the angle in a counter-clockwise direction. If later examination shows that the result of this procedure was not sufficient to normalize pressure, stripping of a neighbouring area of the angle (from 3 to 12) may be undertaken. In the latter case the right eye is rotated two hours in a clockwise direction to make the area accessible. The puncture is made at 10:30 o'clock and stripping is performed from 5 to 3 o'clock in the rotated position which corresponds to 3 to 1 o'clock when the bulbus is in the normal position. It is possible, therefore, by means of two goniotomies to strip the angle up to one-half its circumference, *i.e.*, from the 6 to 12 meridians.

*Preliminary Deepening of the Anterior Chamber with Physiological Saline Solution.* Preliminary deepening of the anterior chamber with physiological saline solution may be performed in cases operated on without the glass in order to minimize the hazard of picking up the root of the iris with the tip of the knife. The chamber is not deepened for the operation under the glass; in this case the blade of the knife is guided under direct vision and therefore picking up of the iris root with consequent haemorrhage can be avoided. Deepening should be considered in infants, especially those between the ages of several days to weeks because of the relatively shallow chamber and narrower angle. It permits of a more deliberate placement of the stripping in regard to its antero-posterior position. However, it is well to dispense with deepening when possible as it introduces a delicate technical detail which, if not adequately performed, may result in leakage of aqueous and postponement of the operation. When deepening is employed great care must be taken in prelaying the corneal puncture. The bulbus is fixed with a Bishop Harman forceps at the opposite limbus. The cornea is punctured very tangentially 1 mm. axial to the corneo-scleral border at 9 o'clock on the right eye and at 3 o'clock on the left eye, with a discission knife, the blade of which has been previously dipped in fluorescein. The wound canal should

be at least 3 mm. long. The tip of the knife should barely perforate Descemet's membrane as observed through a five times magnifying head loupe. It may be necessary to tip the knife backward a little in order to perforate this membrane. Care must be taken not to enlarge the puncture upon removing the dissection knife lest leakage ensue. The puncture made visible by fluorescein is touched with a dry applicator and one dipped in tincture of iodine from which the excess has been removed. With a  $\frac{1}{16}$  30 needle (previously drum tested or examined under a loupe to assure its having a perfect point) attached to a 1.5 c.c. Luer syringe intravenous saline solution is injected, the surgeon fixing the bulbus at the contra-lateral limbus with a Bishop Harman forceps.

### AIR GONIOTOMY

If goniotomies have not reduced the pressure sufficiently and gonioscopy shows that further repetition of goniotomy in the nasal portion of the angle is not feasible because of iris adhesions or scar formation, an attempt may be made to perform a goniotomy under air in the temporal portion of the angle. This area can be made visible by filling the chamber with air.<sup>8,9</sup> Since it is difficult consistently to insufflate the whole anterior chamber with air through a corneal puncture, an oblique scleral incision as for cyclo-dialysis is used and the sterile air injected by means of a curved gold cannula and small Luer syringe. The eye is then fixated with two Gifford forceps with lock and abducted. The temporal limbus disappears behind the canthus. The operator stands on the opposite side. The knife is passed across the bridge of the infant's nose and the cornea punctured 1 mm. axial to the nasal corneo-scleral border. Goniotomy under air or "air goniotomy" of the temporal portion of the angle is performed. Only a gross picture of the insertion of the root of the iris is discernible through air, due to the opacities of the cornea, to reflections and to absence of magnification. However, visibility may be sufficient when combined with familiarity of the angle to act as a guide to the blade of the knife.

*Blunt Dissection.* Blunt dissection of the angle with a spatula inserted through a pre-laid corneal puncture has been tried in place of stripping or peeling of the angle with a goniotomy knife. In practice this has shown no advantage over the present technique with the knife; on the contrary it appears to encourage adhesion of the root of the iris and closure of the angle.

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\* The knife, surgical contact glass and hammer lamp can be obtained from A. H. Parsons Laboratories, 442 Post Street, San Francisco, 2, California. The knife will be obtainable also from E. Grieshaber, Schaffhausen, Switzerland. Recently specifications for its present form have been sent to V. Mueller and to Storz.

*Goniotomy Knife.* The shaft of the knife is conoid in order to prevent loss of aqueous. Its diameter increases progressively from the tip of the blade to the heel of the shaft. The blade is not too sharp as it is used to strip or peel and not to incise, the tip being sharp enough, however, to permit easy puncture of the cornea. Some resistance is felt during the stripping, which gives the operator a feeling of guidance and deliberate movement.

### SUMMARY

Congenital glaucoma in the past has resulted in a high percentage of blindness, due to lack of an adequate operation.

Goniotomy, performed at this writing on 76 eyes afflicted with infantile glaucoma, preserved useful vision in most cases. In 66 eyes pressure was normalized and vision maintained or restored over periods ranging from one to ten years. In ten the operation was unsuccessful. When combined with early diagnosis it provided excellent visual results.

A plea is made for early diagnosis and prompt, adequate operation by goniotomy.

The symptoms of increased intra-ocular pressure in congenital glaucoma may be present at birth, or their onset may be rapid or sudden during the first few months of infancy. In most cases symptoms consist of cloudy cornea, photophobia and other signs of irritation and congestion. Diagnosis should be made as soon as possible after onset of congestive symptoms and not deferred until enlargement of the eye is evident. In the rare cases of slow onset there are no congestive symptoms. Pressure should be measured with a tonometer under ether anaesthesia, which must be sufficient to assure complete relaxation at the moment of measurement.

The appearance of congestive symptoms is prone to lead to a faulty diagnosis of blepharitis, conjunctivitis or keratitis, causing loss of valuable time and bearing tragic consequences.

The initial cloudiness of the cornea is associated with roughening of the corneal epithelium. This disturbance of the cornea is the chief cause of the irritative symptoms and photophobia. If the corneal cloudiness is allowed to persist, it is superseded by permanent scarring with associated irregular astigmatism and ensuing amblyopia of greater or less degree.

Glaucomatous atrophy of the optic nerve was the exception in this series of infants and children. It occurred only in those few cases in which normalization of pressure was unduly delayed. In infants it is not nearly as urgent to protect the optic nerve-head from pressure as it is to relieve cloudiness of the cornea.

If soon after its inception increased intra-ocular pressure is normalized by goniotomy, transparency of the cornea is almost completely restored and maintained, and vision is afforded the opportunity to develop. When this is borne in mind, the urgency of prompt relief of increased pressure is evident.

The mode of action, advantages and disadvantages, indications and contra-indications of goniotomy are given.

The technique of goniotomy is described.

The author wishes to express his appreciation to his colleagues who have referred these patients, as well as to Childrens' Hospital, San Francisco, for its helpful co-operation,

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## THE GOLDMAN ANGLE-REDUCTION PRISM AND GONIOSCOPY CONTACT-GLASS FOR USE WITH A SLIT-LAMP

For slit-lamp examinations of the posterior parts of the eye some means of reducing the angle between the inspection and illuminating beams is required. This want is met by the four-sided prism illustrated herewith (Fig. 1) devised by

Fig. 1

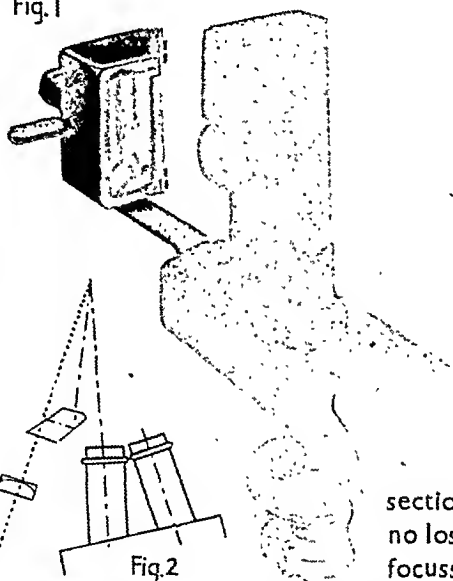


Fig. 2



Fig. 3

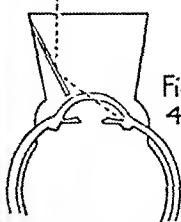


Fig. 4

Prof. Hans Goldman of Berne University, which can be supplied suitably adapted for use on any type of slit-lamp. As will be seen in the diagrammatic illustration (Fig. 2) the prism displaces the angle by  $5^\circ$ , which is usually as much as is necessary. The light beam remains in exactly the same adjustment as when examining the anterior sections of the eye, and there is no loss in the facilities for sharp focussing with the microscope.

For examination of the angle of the anterior chamber Professor Goldman has devised a CONTACT GLASS for use with the angle reduction prism (Fig. 3). The diagrammatic illustration (Fig. 4) shews how it makes possible the examination of the entire iridial angle without any alteration in the adjustment of either the slit-amp or microscope, by rotating it around the corneal axis.

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## COMMUNICATIONS

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### PROGNOSIS IN UVEAL MELANOMA\*†

BY

B. BENJAMIN, J. N. CUMINGS, A. J. B. GOLDSMITH  
*and* ARNOLD SORSBY

THE material recorded in this study represents the total number of cases of uveal melanoma seen at the Royal London Ophthalmic Hospital and at the Royal Eye Hospital, London, during 1925 to 1939, except for a few specimens that could not be traced. In some cases the ultimate outcome was known, but in most the end result had to be ascertained from the records of the Registrar General. This study, therefore, largely hinges on the reliability of such records. It is generally assumed that they are of a high degree of accuracy—an assumption borne out by the fact that a test group of 20 cases, equally divided between those known to

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\* Work carried out with a grant to one of us (A.S.) from the Imperial Cancer Research Fund.

† Received for publication, June 3, 1948.

have died and those known to have survived, checked up accurately against the findings of the Registrar General. In all cases (a total of 285) the type of cell and in all but two cases the amount of pigment contained could be assessed. The investigation of reticulin was restricted to 150 cases. The classification used is largely that employed by Callender and his associates, in which spindle cell A. is Grade 1, spindle cell B. Grade 2, mixed cells Grade 3, and epithelioid cell is Grade 4. A few cases showed spindle cell B. in a fascicular arrangement, and in a few others the cells were necrotic and did not allow of a clear differentiation. Pigment content was assessed as light, medium, or heavy, and reticulin graded as: trace, light, medium, and heavy. Figures 1 to 10 are illustrative.

## 1. STATISTICAL ANALYSIS

### *A Series of 250 Cases of Melanoma of the Choroid*

A detailed analysis is given in the Tables in the Appendix. The following are the salient points:—

1. *Age distribution* (248 cases).—There were no cases in the age group 0—9; there were only 3 cases in the age group 10—19. The subsequent decades gave an increasing number, but 53 per cent. of the total of cases were concentrated in the two decades 50—69. The mean age at excision of the eye was  $53.71 \pm 0.90$ . There was some slight difference in the age incidence as between men and women, but this was not statistically significant, as can be seen from Table I in the Appendix.

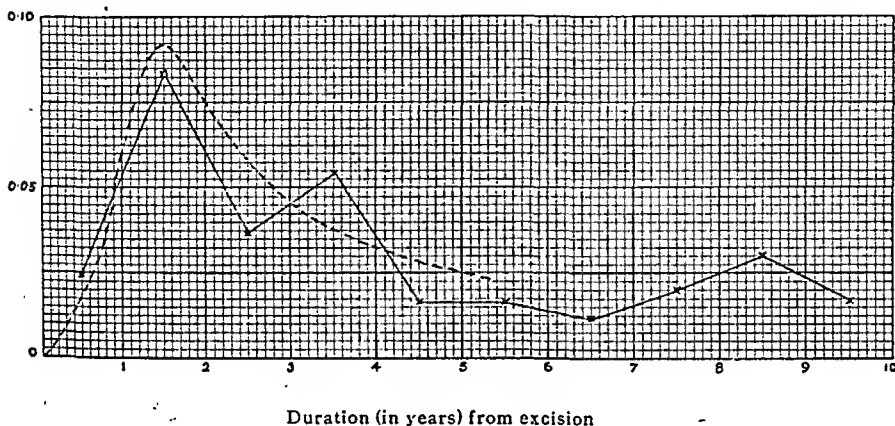
2. *Sex distribution* (250 cases).—No accurate assessment was possible as the relative male and female populations from which the cases were drawn was not known. Indirect computations (as seen in Table II of the Appendix) indicate that there is nothing to suggest that the incidence of melanoma is higher in one sex than in the other.

3. *Histological Components*.—As can be seen from Table III spindle cell B. was the commonest cell type with 59.6 per cent. of the total of cases. Tumours with mixed cells account for 17.6 per cent., and epithelioid cells for 8.8 per cent. Heavy pigment was uncommon accounting for 13.7 per cent., whilst light and medium pigment were fairly equally represented with 41.5 per cent. and 44.8 per cent. each. Heavy reticulin was likewise uncommon (8.3 per cent.); the other extreme—a trace of reticulin—was more common (19.5 per cent.) but light and medium distribution were the most frequent (39.1 per cent. and 33.1 per cent. respectively).

There was little evidence of any definite correlation between

the different histological components, apart from a tendency for tumours with epithelioid cells to be heavily pigmented.

4. *Mortality generally* (250 cases).—The chance of escaping death from metastases in the first five years was 0.822 for males and 0.795 for females, with 0.807 for both sexes combined. The odds declined somewhat if taken for a period of the first ten years, being 0.733, 0.734, 0.734 for males, females and both sexes together respectively (Table IV). The highest mortality occurred in the second year (see graph). Statistically there was no significant sex difference in mortality.



*Central death ratio (m).* (Ratio of deaths from cancer to mean lives exposed during the year). The discontinuous line indicates the underlying trend. In view of the restricted data no attempt was made to fit a curve of a specific mathematical law but an approximation thereto was obtained by drawing a curve through the observed values by graphic graduation.

5. *Effect of age on prognosis* (248 cases).—When three broad age groups were taken—under 40, 40–59, and 60 and over—a statistically significant increase in mortality from metastases with advancing age was observed for the first five years. The odds against the fatal recurrence of cancer shortened from 9:1 to 7:1 between the youngest and oldest age groups (Table V).

6. *Mortality according to type of cell* (250 cases).—No statistical significance could be attributed to the variation in mortality with the different types of cell except for epithelioid cells, the mortality from which was distinctly higher (Table V).

7. *Mortality according to pigment* (248 cases).—A statistically significant lower mortality was found to be associated with a low pigment content (Table VII).

8. *Mortality according to reticulin* (133 cases).—There was a significant correlation between high mortality and low reticulin content (Table VIII).

9. *Mortality by cell and pigment* (248 cases).—Within each pigment group there was little variation with different types of cell apart from epithelioid cells. Within each cell grade low mortality was associated with light pigment content (Table IX).

10. *Cell, pigment and reticulin combinations* (133 cases).—It appears likely that each of the factors has an independent effect on prognosis, but that cell grade is less important than pigment or reticulin. The determination of the partial association of mortality with each of the three factors cannot be reliably made on the data of the present series (Table X).

### *A Series of 30 cases of Melanoma of the Ciliary Body*

In this small series there was no significant difference in age or incidence between the two sexes. The average age of the whole series was  $56.3 \pm 3.1$ . The chance of escaping death from metastases was rather lower than for melanoma of the choroid. The material was not sufficiently extensive to lend itself to detailed analysis.

### *Five cases of melanoma of the iris*

The group consisted of three men and two women. There was one death from metastases in this group. Table XII shows the salient features observed in this small series.

## 2. COMPARATIVE STUDIES ON CHOROIDAL MELANOMA

The considerable literature on prognosis in uveal melanoma is unfortunately largely vitiated owing to the general lack of statistical assessment of the results obtained. Comparative studies of results obtained by different observers also present difficulties owing to the lack of uniformity in criteria used; the older literature is largely inapplicable, particularly since recent studies have shown the significance of reticulin in the assessment of prognosis. Only partial comparison with the variously recorded results is, therefore, possible.

1.—*Age distribution.* The following summary table shows the age distribution in our own series compared with those published by Callender, Wilder and Ash (1942) and Pahwa (1941). The first represents an extensive study covering 1,418 cases observed in the United States. The second deals with 100 cases seen at the Royal London Ophthalmic Hospital between 1930 and 1935—a group covered by our own series.

These three series give essentially the same data: melanoma of the choroid is concentrated in the age groups 40—70.

	Callender, Wilder & Ash. 1,418 cases. per cent.	Pahwa 100 cases. per cent.	Present series. 250 cases. per cent.
0-9	0'14	—	—
10-19	0'92	—	1'21
20-29	5'01	6'3	4'44
30-39	13'33	11'6	12'50
40-49	20'87	22'1	18'55
50-59	26'44	25'3	25'40
60-69	23'13	23'1	27'82
70-79	9'17	11'6	9'27
80-89	0'92	—	0'81
90 and over	0'07	—	—
	100'00	100'0	100'00
Mean age	52'76	53'7	53'71

2.—*Sex distribution.* In 1,550 cases noted by Callender, Wilder and Ash there were 799 men and 751 women. It would appear that their series is not consecutive, but a random selection. In their findings, as in ours, there is nothing to suggest that there is a significant sex difference.

3.—*Cell type.* The following summary table shows the distribution of cell type in the comparable series:—

	Callender, Wilder & Ash.	Pahwa	Terry & Johns	McKee	Present Series.
Spindle A. ...	35	22	6	14	11
Spindle B. ...	117	7	12	—	149
Mixed ...	276	29	31	2	44
Epithelioid ...	14	25	8	7	22
Fascicular ...	13	9	8	4	18
Necrotic ...	45	—	—	—	6
	500	92	65	27	250

The series given by Callender, Wilder and Ash and also that of Pahwa and of Terry and Johns contained a high proportion of mixed tumours reducing the proportionate incidence of other cell

types. Our series shows a high incidence of spindle B. types. The proportion of epithelioid cell tumours in our series is distinctly higher than in the American series, though lower than in the other small series.

4.—*Pigment.* The following summary table shows the comparative incidence of pigment in a series recorded by Callender, Wilder and Ash, and by ourselves:—

	Callender, Wilder & Ash.	Present Series.
<i>Pigment</i>		
Light	141	103
Medium	235	111
Marked	111	} 34
Heavy	13	
	500	248

It will be noted that there is a greater incidence of marked and heavy pigment in the first series.

5.—*Reticulin content.* The significant studies on reticulin are those that have come from Callender and his associates. The small series of 41 cases published by McGregor and Hill does not lend itself to statistical assessment; their general conclusion that a low reticulin content is disadvantageous is also brought out in the 61 cases recorded by Pahwa. The distribution of reticulin in the series by Callender, Wilder and Ash, and our own, are shown in the following summary table:—

Reticulin content	Callender, Wilder & Ash	Present Series.
Heavy	19	} 11
Marked	90	
Medium	143	44
Light	223	52
Absent	25	26*
	500	133

\*Absent or trace.

Our series would appear to contain more cases with low reticulin content.

6.—*Prognosis in general.* As different series of cases appear to contain different proportions of the constituent histological elements it would seem that the assessment of prognosis is difficult unless one is sure that the various series are comparable and unselected. Moreover, the time at which the affected eye was removed may vary in different statistical computations. Our own series gives a distinctly good prognosis, the survival rate for a period of five years being 80·7 per cent., and 73·4 per cent. for ten years. Callender, Wilder and Ash (1942) give a survival rate of 52 per cent. for five years and 34 per cent. for ten years, but their findings are open to the statistical criticism that they have not dealt with the cancer mortality within a definite period. Martin-Jones, likewise, obtained a poorer prognosis than our series shows. His survival rate for a period of five years is 64·2 per cent., and for a period of ten years 44·5 per cent. Recalculating his data on the basis of chance of escaping death from cancer during X years following excision, his percentages are raised nearer to ours, being 67·2 and 53·0 respectively. Pahwa's total mortality from secondary growth (for material overlapping ours, but in which mortality was assessed by direct enquiry) approaches ours still more closely. Closer still is the mortality of about 26·5 recorded by Hippel (1930) in a collected series of 609 cases.

7.—*Prognosis in relation to histological components.* Callender, Wilder and Ash found that prognosis varies directly with cell type, pigment content and reticulin content. For a five-year period there was a mortality of 6 per cent. with spindle cell A., 25 per cent. with spindle cell B., 62 per cent. with mixed tumours and 71 per cent. with tumours composed of epithelioid cells; tumours with spindle cell B. in fascicular arrangement and those with necrotic cells gave a mortality of 38 per cent. and 49 per cent. respectively. The mortality from tumours containing light, medium, marked and heavy pigment was respectively 34, 51, 55 and 69 per cent. Mortality decreased with increase of reticulin content. It was 80 per cent. when reticulin was absent, and 55, 44, 36 and 10 per cent. when the reticulin content was light, medium, marked and heavy respectively. It is unfortunate that their assessment is not made by a statistical analysis which takes account of period of observation. Our own findings are distinctly more limited: a statistically significant increased mortality in relation to epithelioid cells, a lower mortality with light pigment content, a higher mortality with low reticulin content.



8.—*Age in relation to prognosis.* Callender, Wilder and Ash suggest that the worse prognosis is in the higher age group. Martin-Jones also finds a less favourable prognosis at older ages. Our statistical evaluation shows the same trend.

### 3. DISCUSSION

Judging by the older literature, prognosis in uveal melanoma has improved steadily during the last seventy years. Thus, Hirschberg gives the survival rate as 25 per cent. in 1882, 35 per cent. in 1895, and 56 per cent. in 1903. References to further data of this type are given by v. Hippel (1930) and Teraskeli (1928). Continental studies have been largely concerned with the stage of growth and its bearing on prognosis, stage I representing the phase when the tumour is confined to the uveal tract, stage II when it has penetrated into the ocular tunics, and stage III when it has perforated these. (In another classification stage I is the quiet eye, stage II the secondary glaucomatous process, stage III orbital invasion, stage IV dissemination.) Studies on these lines have led to rather sterile discussions as to the best time for removing the affected eye. The great merit of Callender's work at the American Registry of Ophthalmic Pathology is that in the first place he introduced an adequate classification (and possible grading) of cell type (Callender, 1931), and that secondly he established the significance of reticulin as a prognostic factor in uveal melanoma (Callender and Wilder, 1935). These excellent pathological studies, recorded in three successive papers, covered at first 111 cases (Callender, 1931), subsequently 253 cases (Wilder and Callender, 1939), and more recently 500 cases (Callender, Wilder and Ash, 1942). It is unfortunate that in rightly stressing the need for adequate histological detail, Callender and his associates have tended to overlook the grosser—but necessary—criteria implied in the classification by stages.

Our data do not suggest that there is any correlation between the three histological components, except that tumours with epithelioid cells tend to be heavily pigmented. Since heavy pigmentation is regarded as an unfavourable prognostic feature, the unfavourable effect of epithelioid cells is emphasized.

If choroidal melanomata are therefore to be regarded as consisting of three freely variable components, it is clear that prognosis must be assessed on the basis of each of the components. In addition, the behaviour of the tumour as a whole must also be taken into account. As long as a true measure of prognosis is not available it is impossible to indicate whether exenteration

*Figs 1-4 to illustrate cell types*

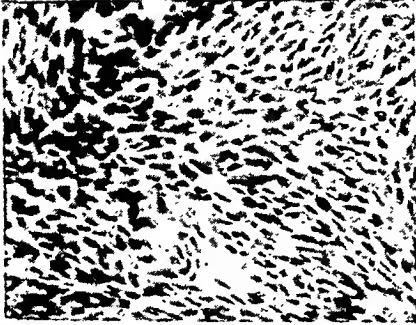


FIG. 1 Spindle cell A  
(Magnification  $\times 160$ )

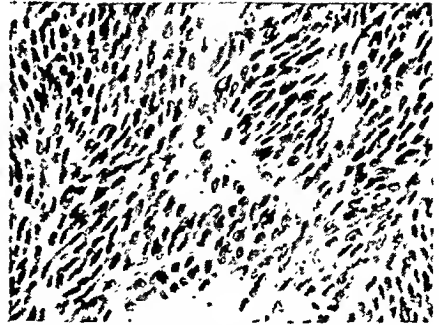


FIG. 2. Spindle cell B  
(Magnification  $\times 160$ )

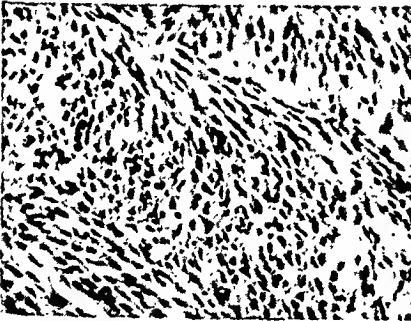


FIG. 2a. Spindle cell B, fascicular  
arrangement (Magnification  $\times 160$ )

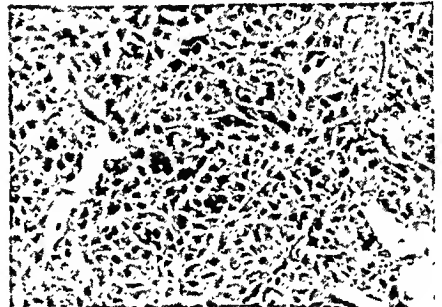


FIG. 3. Mixed cells  
(Magnification  $\times 160$ )

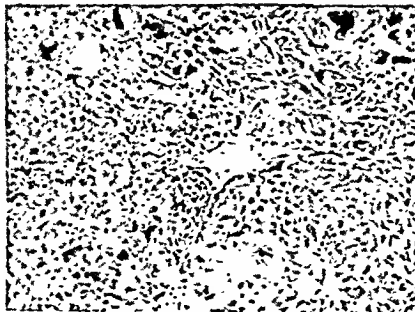


FIG. 4. Epithelioid cells  
(Magnification  $\times 80$ )

*Figs. 5-7 to illustrate pigment content. Figs. 8-10 to illustrate reticulin content*

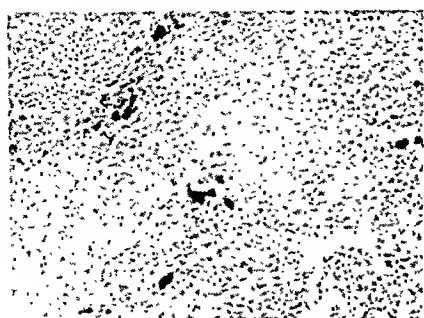


FIG. 5. Light pigment content  
(Magnification  $\times 80$ )

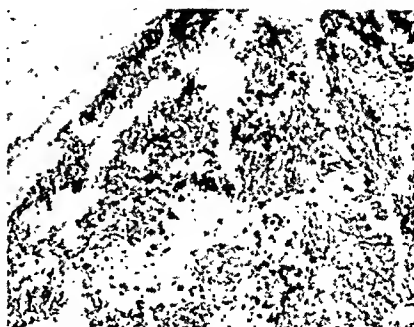


FIG. 6. Medium pigment content  
(Magnification  $\times 40$ )

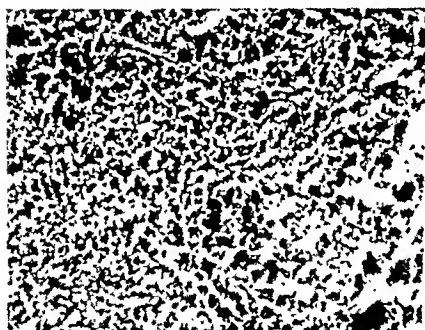


FIG. 7. Heavy pigment content  
(Magnification  $\times 40$ )



FIG. 8. Light reticulin content  
(Magnification  $\times 40$ )



FIG. 9. Medium reticulin content  
(Magnification  $\times 40$ )



FIG. 10. Heavy reticulin content  
(Magnification  $\times 40$ )

of the orbit rather than excision of the globe, or possibly radiotherapy, is the proper treatment. It would seem essential that in the further collection of pathological material uniform criteria should be employed. These criteria might well be:—

(i) Histological. The classification employed by Callender and his associates is eminently satisfactory for cell type. The grouping of pigment into four quantitative groups is probably an unnecessary refinement; in practice a classification into light, medium and heavy is easier and probably more reliable. Likewise with reticulin: the distinction between marked and heavy seems unnecessary and rather troublesome.

(ii) Gross features in the tumour. Vascularity, haemorrhage and necrosis all need to be noted.

(iii) Extension beyond the uvea. Extension into the ocular tunics, the emissary vessels and into the orbit also need to be recorded.

The classification into stages is now largely a matter of historical interest. Eyes with melanoma of the choroid are generally removed in what constituted stage I, so that as many distinctive components as possible in addition to histological features have to be isolated and studied. It should be redundant—but nevertheless it appears to be necessary—to add that proper statistical evaluation of the collected material is also essential.

### Summary

(1) A series of 250 cases of melanoma of the choroid, 30 cases of melanoma of the ciliary body, and 5 cases of melanoma of the iris was studied histologically and correlated with mortality from metastases.

(2) Fifty-three per cent. of all cases of choroidal melanoma were concentrated in the two decades 50–69 years. The mean age at excision of the eye for the whole series was  $53.71 \pm 0.90$ . There was no statistically significant sex difference in age distribution or incidence. Histologically spindle cell B. predominated, accounting for 59.6 per cent. of the total of cases. Spindle cell A. accounted for 4.4 per cent., mixed cells for 17.6 per cent., epithelioid cells for 8.8 per cent., spindle cell B. in fascicular arrangement for 7.2 per cent., and necrotic tumours for 2.4 per cent. Heavy pigment was present in 13.7 per cent., whilst light and medium pigment distribution gave 41.5 and 44.8 per cent. respectively. Reticulin, studied in 133 cases, was present in heavy amounts

in only 8.3 per cent. A trace of reticulin was present in 19.5 per cent., whilst light and medium reticulin distribution was observed in 39.1 per cent. and 33.1 per cent. respectively. Apart from a statistically significant association of heavy pigment with epithelioid cells, there was no evidence of any other correlation between the histological components. The chance of escaping death from metastases in the first five years was 0.807 for the series as a whole, declining to 0.734 for a period of ten years. The highest mortality occurred in the second year after excision. There was a statistically significant better prognosis in the younger age groups. No statistical significance could be attributed to variation in mortality with different types of cells, except that epithelioid cells carried a worse prognosis. A low mortality was found associated with a low pigment content, and a high mortality with low reticulin content. Each of the three histological components appears to have an independent, but not equally forcible, effect on prognosis, so that mortality is influenced to some extent by cell grade, but more by pigment and reticulin content. The main prognostic factors as they emerge from this study are: a favourable effect from light pigment content, and an unfavourable effect from epithelioid cells and from low reticulin content. These general conclusions support the findings of Callender and his associates, though they are not as emphatic as theirs.

(3) A study of the 30 cases of melanoma of the ciliary body suggests that mortality from this type of tumour is rather higher than for melanoma of the choroid.

(4) The importance of studying the stage of development of the tumour in addition to its histological features is stressed.

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## APPENDIX—STATISTICAL ANALYSIS

## 1.—Melanoma of the choroid

1. *Age distribution.*—Table I shows the sex and age distribution of the series at excision, together with the mean ages and standard deviations.

TABLE I—*Sex and age distribution of cases of melanoma of the choroid.*

Age	Males	Females	Total	
			No.	Per cent.*
0 —	—	—	—	—
10 —	2	1	3	1'21
20 —	4	7	11	4'44
30 —	11	20	31	12'50
40 —	18	28	46	18'55
50 —	32	31	63	25'40
60 —	34	35	69	27'82
70 —	13	10	23	9'27
80 —	1	1	2	0'81
Not stated	1	1	2	—
Total	116	134	250	100'00
Mean age	55'26 ± 1'31	52'37 ± 1'22	53'71 ± 0'90	

\* Based on 248 stated cases only.

In the actual samples the mean age at excision is less for females than for males, but this difference is not statistically significant and there is no evidence of association between sex and age.

The analysis of the variance of age is as follows:—

	Degrees of freedom	Sum of squares	Mean square
Between sexes	1	515'98	515'98
Residual	246	48,671'12	197'85
	247	49,187'10	

The probability that the difference in variance estimates is attributable to sampling fluctuation exceeds 0.10.

The mean age at excision may therefore be estimated at 53.71 ± 0.90 years.

2. *Sex distribution.*—The relative male and female populations from which the cases were drawn is not known and therefore the sampling error of the numbers for each sex cannot be accurately assessed, but it will be seen from Table II that the ratio of male to female cases in any age group is not inconsistent with that operating in the general population of England and Wales.

TABLE II—*Sex incidence.*

Age	Male cases	Ratio of females to males in England and Wales census 1931	Expected female cases on basis of census ratios	Actual female cases	Actual — expected	Approx. standard error of expected female cases <sup>a</sup>
10 —	2	0.995	1.99	1	— 0.99	1.40
20 —	4	1.059	4.23	7	+ 2.77	2.11
30 —	11	1.157	12.72	20	+ 7.28	3.84
40 —	18	1.160	20.87	28	+ 7.13	4.92
50 —	32	1.115	35.69	31	— 4.69	6.31
60 —	34	1.159	39.41	35	— 4.41	6.76
70 —	13	1.360	17.69	10	— 7.69	4.91
80 —	1	1.782	1.78	1	— 0.78	1.78
Not stated	1	—	1.09	1	— 0.09	1.09
Total	116	1.088	127.31	134	+ 6.69	11.72

<sup>a</sup> On assumption stated in text.

In the above table the variance in the expected female cases due to the application of the census ratios to the unknown portion of the population included in the sample is ignored, and account is taken only of the sampling error of the number of male cases in each group. The standard error in the estimate of the female cases arising from this is shown in the final column and is taken as approximately  $r \times \sqrt{M}$  where  $r$ =census sex ratio,  $M$ =actual male cases. It will be seen that the excess or deficiency in the actual female cases in any age group is in no instance greater than twice this standard error. The systematic character of the differences in the penultimate column of the table (at first positive then negative) reflects the fact that the females are as a group younger than the males in this series, though this difference has been shown not to be statistically significant. It would appear that the incidence of melanoma cannot be regarded as any greater in one sex than the other.

TABLE III—*Histological Components.*

	Males	Females	Persons	Percentage
Cell type (250 cases)				
Spindle Cell A. ...	5	6	11	4.4
Spindle Cell B. ...	71	78	149	59.6
Mixed ...	17	27	44	17.6
Epithelioid Cell ...	10	12	22	8.8
Spindle Cell B. fascicular	12	6	18	7.2
Necrotic ...	1	5	6	2.4
				100.0
Pigment (248 cases)				
Light ...	49	54	103	41.5*
Medium ...	52	59	111	44.8*
Heavy ...	14	20	34	13.7*
				100.0
Reticulin (133 cases)				
Trace ...	11	15	26	19.5*
Light ...	26	26	52	39.1*
Medium ...	23	21	44	33.1*
Heavy ...	5	6	11	8.3*
				100.0

\* Of stated cases.

3. *Histological components.*—The type of cell could be established in all cases, the degree of pigmentation in all but two cases, and reticulin content in 133 cases. The sub-joined table shows the findings obtained.

The possibility of association between the three components was investigated by independence tests of the chi square type. There appeared to be a significant association of heavy pigment content with epithelioid cells, but no other significant finding emerged.

TABLE IV—*Survivorship factors.*

Year of survival	Males			Females			Both sexes combined		
	Mean exposed	Deaths from metastases	Chance of escaping death from cancer	Mean exposed	Deaths from metastases	Chance of escaping death from cancer	Mean exposed	Deaths from metastasis	Chance of escaping death from cancer
x	E	θ	P <sub>x</sub>	E	θ	P <sub>x</sub>	E	θ	P <sub>x</sub>
0 —	113	4	0·965	132	2	0·985	245	6	0·976
1 —	106·5	6	0·945	123·5	13	0·900	230	19	0·921
2 —	99	6	0·941	115·5	2	0·983	214·5	8	0·963
3 —	93·5	2	0·979	109·5	9	0·921	203	11	0·947
4 —	89	2	0·978	104·5	1	0·991	193·5	3	0·985

Chance of escaping death from cancer in the first five years :—

0·822

0·795

0·807

5 —	84·5	1	0·988	102·5	2	0·981	187	3	0·984
6 —	78	—	1·000	95·5	2	0·979	173·5	2	0·989
7 —	68·5	2	0·971	84·5	1	0·988	153	3	0·981
8 —	59·5	2	0·967	75	2	0·974	134·5	4	0·971
9 —	49·5	2	0·960	66·5	—	1·000	116	2	0·983

Chance of escaping death from cancer in the first ten years :—

0·733

0·734

0·734

The survivorship factor  $P_x = \frac{2 - M}{2 + M}$  — where  $M = \frac{\theta}{E}$ , and the chance of escaping death from cancer during the first five or ten years is given by the product of the first five or ten of the series of values of  $P_x$ .

4. *Mortality generally.*—The cases have been analysed according to the number of years observed since excision. The deaths from metastases occurring between  $x$  and  $x \pm 1$  years after excision have been related to the mean number of patients exposed to risk of death from cancer during that year leading to the calculation of the chance of escaping death from cancer in each of the consecutive years following excision. The principal details (up to 10 years) are shown in Table IV.

The difference between the five year factors for males and females is not significant, as will be seen from the following test.

	Mean exposed E	Deaths from metastases θ	Central death rate $\frac{M - \theta/E}{M} = \theta/E$	Expected deaths $\theta^1 = E \times M$	$\theta - \theta^1$	$\frac{(\theta - \theta^1)^2}{E \times M(1 - M)} = \chi^2$
Males	100·2	20	(both sexes)	21·68	— 1·68	0·166
Females	117·0	27	—	25·32	+ 1·68	0·142
Total	217·2	47	0·2164	—	—	0·308
						P = 0·58



In calculating the exposed to risk for any particular year, deaths whether from metastases or from other causes were given six months' exposure.

The graph, in the text illustrates the variation of the risk of death from metastases according to duration after excision. The continuous curve connects the observed values of the ratio of deaths from metastases in each year to lives exposed during the year (M) (both sexes combined). The irregularity is, of course, inevitable in view of the small numbers involved. The general trend is indicated by the discontinuous line. In view of the restricted data no attempt was made to fit a specific mathematical law, but an approximation thereto was obtained by drawing a curve through the observed values by inspection. The risk of metastases rises to a peak in the second year and thereafter falls fairly rapidly.

5. *Effect of age on prognosis.*—The chance of escaping death from metastases during the first five years following excision was calculated separately for each of three broad age groups—under 40, 40-59, 60 and over. A statistically significant increase in mortality with advancing age takes place as indicated in the following table.

TABLE V—*Mortality in age groups—first five years.*

Age group	Mean lives exposed	Deaths from metastases	Expected deaths on the assumption of no association with age.	Actual — expected	Chance of escaping death from cancer.
Under 40 ...	42.5	4	9.16	— 5.16	0.910
40 — 59 ...	100.5	15	21.67	— 6.67	0.861
60 and over ...	75.0	28	16.17	+ 11.83	0.685

Using Yates' correction —  $\chi^2 = 15.38$   $P < 0.0005$ .

There were no significant differences between the two sexes in any age group.

It will be seen that the odds against the recurrence of cancer in the first five years shorten from 9:1 to 7:1 between the youngest and the oldest age group.

6. *Mortality according to type of cell.*—In Table VI the mortality data for the first five years are analysed according to the cell type of the melanoma, and actual deaths from metastases in each group are compared with those expected on the assumption that mortality is not associated with cell.

TABLE VI—*Cancer mortality by cell grade — first five years (both sexes combined).*

Grade of cell	Mean lives exposed	Deaths from metastases	Expected deaths (assuming no association with cell grade)	Actual — Expected
1 (Spindle A) ...	10.5	1	2.24	— 1.24
2 (Spindle B) ...	131.5	25	28.09	— 3.09
3 (Mixed) ...	39.0	8	8.33	— 0.33
4 (Epithelioid) ...	17.5	8	3.74	+ 4.26
2 Fascicular ...	16.5	3	3.53	— 0.53
Necrotic... ..	5.0	2	1.07	+ 0.93
Total... ..	220.0*	47	47.00	—

\*This differs from the average in Table IV because for the purpose of the above table the data are not analysed according to the individual years of the period.

Of the differences in the final column of this table that for Grade 4 alone can be regarded as statistically significant. Comparing the cancer mortality in this grade with that of the remainder, we find  $P_x^2 = 0.0096$ .

7. *Mortality according to pigment.*—When the melanomata are classified by pigment the mortality experience in the first five years is as shown in Table VII.

TABLE VII—*Mortality by pigment—first five years*  
(both sexes combined).

Pigment-	Mean lives Exposed	Actual deaths from metastases	Expected deaths (assuming no association with pigment)	Actual — Expected
Light ... ..	94.5	9	19.16	— 10.16
Medium ... ..	92.5	28	18.76	+ 9.24
Heavy ... ..	30.0	7	6.08	+ 0.92
Total ... ..	217.0	44	44.00	—

$$\chi^2 = 12.64$$

$$P = 0.002$$

It appears that lower mortality is associated with light pigment.

8. *Mortality according to reticulin content.*—The reticulin content was not stated in all cases and the mortality data are scanty, but the following analysis suggests that higher mortality is associated with low reticulin content. The

TABLE VIII—*Mortality by reticulin content first five years*  
(both sexes).

Reticulin	Mean lives exposed	Actual deaths from metastases	Expected deaths (assuming no association with reticulin content)	Actual — Expected
Trace or light ... ..	61.5	26	15.65	+ 10.35
Medium ... ..	41.0	2	10.43	— 8.43
Heavy ... ..	11.5	1	2.92	— 1.92
Total stated ... ..	114.0	29	29.00	—

differences between actual and expected deaths for the first two groups are greater than twice the standard errors involved, and the differences are significant.

9. *Mortality by cell and pigment.*—In Table IX the mortality experience in the first five years is subdivided according to cell grade and pigment and the ratios of deaths to lives exposed are given. The numbers involved are small and in only a few cases which have been underlined do the ratios differ significantly from that based on total deaths and total exposures.

In the "light pigment" group, the ratios for the different cell grades are very close to that for the "light pigment" group as a whole with the exception of grade 1 and the necrotic type where there were no deaths and grade 4 where the ratio was higher though not significantly. For medium pigment there is uniformity except for grades 4 and 2—fascicular where the ratios are higher than that for the medium pigment group as a whole (significant for grade 4). For heavy pigment, grade 4 alone shows a ratio higher (though not significantly so) than the group ratio. Within each pigment group therefore there is very

TABLE IX—*Mortality from metastases by cell and pigment first five years (both sexes combined).*

Cell grade	Pigment											
	Light			Medium			Heavy			Total		
	E	$\theta$	M	E	$\theta$	M	E	$\theta$	M	E	$\theta$	M
1 ... ..	6	—	—	3.5	1	0.29	1	—	—	10.5	1	0.10
2 ... ..	62.5	6	0.10	53.0	14	0.26	14	2	0.14	129.5	22	0.17
3 ... ..	11.5	1	0.09	20.5	6	0.29	6	1	0.17	38	8	0.21
4 ... ..	3	1	0.33	8	4	0.50	6.5	3	0.46	17.5	8	0.46
2 Fascicular ...	10.5	1	0.10	4	2	0.50	2	—	—	16.5	3	0.18
Necrotic ...	1	—	—	3.5	1	0.29	0.5	1	2.0	5	2	0.40
Total ... ..	94.5	9	0.10	92.5	28	0.30	30	7	0.23	217	44	0.20

(1) E = mean exposed.  $\theta$  = deaths metastases. M =  $\theta/E$ .

(2) Discrepancies with Table 6 are due to the exclusion of cases in which the pigment is not stated.

little variation of mortality with cell grade apart from grade 4. On the other hand when the effect of pigment within each cell grade is inspected it will be seen that low mortality is associated with light pigment in every instance.

This analysis suggests that while the observation of light pigment is by itself an indication of light mortality, no inference as to mortality may be drawn from cell grade alone (except perhaps for grade 4); it is necessary also to determine the pigment.

10. *Cell, pigment and reticulín combinations.*—The numbers were too small to bring reticulín into account in the above mortality analysis, but Table X shows the analysis of the whole series by cell, pigment and reticulín content excluding those in which all three factors were not recorded.

TABLE X—*Analysis of series according to cell, pigment, reticulín.*

Reticulín	Cell 1 Pigment			Cell 2 Pigment			Cell 3 Pigment			Cell 4 Pigment			Cell 2 Fascicular Pigment			Necrotic Pigment			Total Pigment		
	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Trace or light	2	1	1	24	11	7	3	4	3	2	4	3	8	2	2	—	—	1	39	22	1
Medium	1	1	—	12	19	—	3	2	2	—	1	1	1	1	—	—	—	—	17	24	—
Heavy	2	—	—	4	3	1	—	—	—	—	—	—	1	—	—	—	—	—	7	3	—
Total	8			81			17			11			15			1			133		
Per cent. "Trace or light"	50			52			59			82			80			(100)			59		

If these figures are representative of the whole series, the following inferences may be drawn:—

(i) It might be suggested that the high mortality in epithelioid cell-type cases was due to light reticulín content. A rough test can be made from Table X,

assuming that these figures (which are only a fraction of the total exposed-to-risk in the series) are yet representative of the whole series.

Considering the distribution of Table X, viz.:—

Reticulin	Cells					Total
	1	2	3	4	F+N	
L	4	42	10	9	13	78
M	2	31	7	2	2	44
H	2	8	—	—	1	11
	8	81	17	11	16	133

If these numbers were exposed to the mortality of Table VIII, *i.e.*, if the reticulin content were the only factor and mortality was unaffected by cell-type, we should get the following expected deaths and death-rates:—

*Expected deaths on reticulin mortality.*

Reticulin	Cells				
	1	2	3	4	F + N
L	1·7	17·8	4·2	3·8	5·5
M	0·1	1·5	0·3	0·1	0·1
H	0·2	0·7	—	—	0·1
	2·0	20·0	4·5	3·9	5·7
Hypothetical mortality rates	0·25	0·25	0·26	0·35	0·36
Actual rates (Table 6)	0·10	0·19	0·21	0·46	0·23

There is a substantial difference between "hypothetical" and actual rates in cell grade 1 and in the fascicular-necrotic group, though it has to be borne in mind that the actual rates are here based on small numbers. On the whole the impression is gained that the cell grade may be an independent factor in prognosis but is not such an important one as reticulin or pigment. This is not a conclusive finding, however, and requires confirmation.

(ii) In the pigment groups the percentages with "trace or light reticulin" are as follows:—

Light pigment	...	...	62
Medium "	...	...	45
Heavy "	...	...	79

The mortality experience of the light pigment group is not, therefore, explicable on the hypothesis that the reticulin with which it is associated is the causative factor, as this would lead to the expectation of heavier mortality in the light pigment group than in the medium pigment group instead of the lighter mortality actually observed.

(iii) Conversely the heavy mortality associated with light reticulin does not arise from association between reticulin and pigment or cell. If the rates of Table IX are weighted with the proportions of Table X, the death-rates for the reticulin groups, if cell grade and pigment were the only operating factors, would be as shown below. The *actual* rates are quite different.

	Central death-rate ( $\theta/E$ )	
	" Expected "	Actual
Trace or light reticulin...	0.20	0.42
Medium ... ..	0.21	0.06
Heavy ... ..	0.13	

(iv) It appears likely that each of the factors has an independent effect on prognosis but that cell grade is less important than pigment or reticulin content. The determination of the partial association of mortality with each of the three factors cannot be reliably made on the data of the present series.

## 2.—Melanoma of the ciliary body

1. *Age and sex distribution.*—There were only 30 cases in this series, the age and sex analysis being as follows:—

Age	Males	Females
20—	1	2
30—	2	1
40—	2	2
50—	3	2
60—	3	5
70—	3	3
80—	1	—
Total	15	15

There is no significant difference in age or incidence between the two sexes. The average age of the whole series is  $56.3 \pm 3.1$ .

2. *Mortality.*—The chances of escaping death from metastases in the first five and ten years following excision, calculated in the same way as for melanoma of the choroid (except that individual years of the periods were not observed separately), are as set out below:—

Chance of escaping death from metastases in X years.

X	Males	Females	Both sexes
5	0.459	0.739	0.601
10	0.345	0.484	0.412

Differences in these factors between males and females arise in the first five years. The details are:—

Years	Males			Females			Difference between sexes
	Mean exposed $\frac{E}{\theta}$	Deaths from cancer $\frac{\theta}{\theta}$	$M = \theta/E$	Mean exposed $\frac{E}{\theta}$	Deaths from cancer $\frac{\theta}{\theta}$	$M = \theta/E$	
0 — 4	10.8	8	0.741	13.3	4	0.301	Significant
5 — 9	3.5	1	0.286	7.2	3	0.417	Not significant

It appears that metastases occurred later in females than in males.

In such a small series, the sampling errors arising in an analysis of mortality by cell grade or pigment or reticulin content were relatively large, and no statistically significant variations were found.

3. *Histological components.*—The following summary table gives the salient features observed:—

TABLE XI—*Ciliary Body: distribution of histological components.*

	Cell grade					Pigment			Reticulin				
	1	2	3	4	2 Fasc.	Light	Medium	Heavy	Trace	Light	Medium	Heavy	Not stated
M.	1	7	4	3	—	4	9	2	2	3	2	—	—
F.	1	7	2	2	3	6	3	6	4	3	2	—	—
P.	2	14	6	5	3	10	12	8	6	6	4	—	14

The distribution of these components is not substantially different from that observed in choroidal melanoma.

### 3.—Melanoma of the iris

The following summary table gives the available information on the five cases in this series:—

TABLE XII—*Findings in five cases of melanoma of the iris.*

	Age	Cell	Pigment	Reticulin	Outcome
Males	18	Spindle B.	Medium	Not stated	Alive 6 years later.
	51	" "	" "	" "	Alive 20 years later.
	71	" "	Heavy	Heavy	Alive 14 years later.
Females	52	Spindle B.	Light	Not stated	Died from metastases within 2 years.
	60	" "	Medium	" "	Died 12 years later from cerebral thrombosis.

The one case with death from metastases was vascular histologically.

DOUBLE STAINING FOR BULK SPECIMENS OF  
RETINA AND CHOROID\*

BY..

ARNOLD LOEWENSTEIN

FROM THE TENNENT INSTITUTE OF OPHTHALMOLOGY  
UNIVERSITY GLASGOW (PROFESSOR W. J. B. RIDDELL)

PUBLICATIONS from the Tennent Institute (A. J. Ballantyne, 1941) have shown that in the anatomical investigation of pathological fundus changes, unless we follow a certain routine we run the risk of missing essentials. Slit-lamp examination of the optic nerve and retina is the first step. Ample use of the clearing method of retinal tissue is the second in the scheme described by Loewenstein, 1942.

This method made possible the discovery of microaneurysms in the retina of diabetics with no signs of retinopathy (A. J. Ballantyne and A. Loewenstein, 1944; *a* and *b*).

Study of the cleared unstained retina in bulk was a great help in the investigation of hypertensive retinopathy, of new formed intra-, pre- and retro-retinal vessels, of thrombotic changes, of vasculitis retinae, and many other diseases of the eye. It also led the way to the discovery of "cushion cells" in the capillaries, and of intramural vessels in the retinal vascular system (Loewenstein, 1946 and 1948).

The cleared unstained retina and choroid in bulk revealed a multitude of details.

But one of the greatest advantages of this method, which could be called the "simplest type of microscopical investigation," is undoubtedly the surview it provides of different pathological appearances, without inhibiting the study of the finest details. Thus, the close linkage of several changes became manifest in this simple manner, a linkage which could only have been proved otherwise by painstaking reconstruction of serial sections.

The range of detail we are able to perceive in unstained cleared specimens is increased if we make ample use of reduced illumination by closing down the iris diaphragm, and by dark adaptation of the observer. On the other hand, some parts of the specimen may demand more light. Microscopy of unstained bulk specimens cannot be approached in the "static" manner reserved for stained sections. It has to be performed "dynamically," one hand always being on the iris diaphragm.

And, last but not least, patience and far more time are required for a single specimen, as we are dealing with a tissue of considerable

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thickness. We therefore focus different layers. If we assume the thickness of a normal histological section to be  $10\mu$  we are investigating a tissue of approximately ten times the usual thickness, and each layer of about  $10\text{--}20\mu$  thickness has to be studied separately. Our work is three dimensional in contrast to the usual two dimensional routine microscopy. The use of a binocular eyepiece is recommended. Use of the phase microscope promising.

In spite of the improvements achieved, I soon felt that staining might increase contrasts, and add something to the elucidation of retinal anatomy. I have used a great many stains since I started this work eight years ago, without the desired result. Recently, more satisfactory results were obtained since I returned to haematoxylin and used a prolonged overstaining with a dilute solution, and washed in tapwater for ten minutes after careful removal of the vitreous with cotton wool. The specimen is placed into a stain consisting of 2—4 drops of the stock solution of haematoxylin in 5 ml. tapwater, and left in this solution 4—6 hours or longer at room temperature. Control under the microscope until overstaining is achieved. The specimen must appear dark bluish in water, and not translucent enough to distinguish details.

This staining sufficed to show beautifully the dark concentric lines in a case of pressure folds caused by a retrobulbar metastatic tumour. It shows ganglion cell distribution of the macular area and the nerve fibre pattern perfectly.

After rinsing in water, fat staining of the specimen is performed with Sudan IV. I now use the Kay and Whitehead technique with a stock solution in which 2 g. Sudan IV powder is dissolved in one litre of absolute ethyl alcohol at room temperature. It is boiled gently till all the powder is dissolved.

To 7 ml. of this stock solution, 9 ml. 50 per cent. alcohol is added. It is left at room temperature for an hour and filtered. The specimen is put into the filtrate and kept forty-five minutes in the incubator at  $37^{\circ}\text{C}$ . The specimen is washed in distilled water and examined in 50 per cent. glycerine.

I have abandoned the earlier used Spielmeyer technique, in which the specimen is heated till vapours rise. This higher temperature might do harm to the fine retinal structure, and specially to the distribution of fat.

If it is to be kept permanently, it can be framed with tempera or mounted in glycerine jelly to which several crystals of carbolic acid are added to keep off mould infection. This may still occur, unfortunately, after some years, in spite of carbolic acid addition.

The nuclei appear dark purplish, the whole vascular system standing out clearly in the purple mass of ganglion cells, and



nuclei of the inner nuclear layer. If we want to study the deepest retinal layers we turn the specimen upside down. We may achieve the same effect with a dry specimen turning the whole slide. The use of the highest powers of the microscope will depend then on the thickness of the used glass slide, and the focal distance of the front lens in the microscopic objective.

The capillaries are seen in their course, both the superficial network and the deeper one. It is interesting to observe the linkage between the two systems.

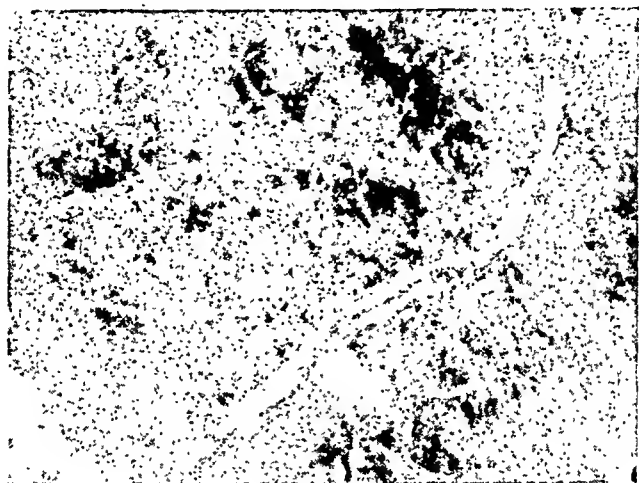


FIG. 1.

Hypertensive retinopathy. Retina in bulk. Haematoxylin.  $\times 300$  approx. Note the multitude of dilated capillaries (aneurysms). Hyaline thickening of vascular walls.

All calibre variations are sharply visible, spherical and spindle-shaped dilation stand out clearly (Fig. 1). They are of enormous frequency in different vascular retinal diseases.

Photomicros are unable so far to reproduce the fullness of the stereoscopic impression; sketches combining the images of different focus are more suitable.

Fatty changes of the vessel walls present a lively contrast shining red against the dark blue of the nuclei. Fatty aneurysms are frequent—they are convincing if we find them linked with a fatty capillary like a grape (Fig. 2). We found fatty aneurysms in diabetic eyes, sometimes with blood-filled dilatation of the venules, sometimes without "red" aneurysms. They are even more frequent in cases of thrombotic occlusion of the central vein. Sub-endothelial fatty necrosis is frequent as well, and is easily recognised in arteriosclerosis and atheromatosis, often found side by side in the same retina.

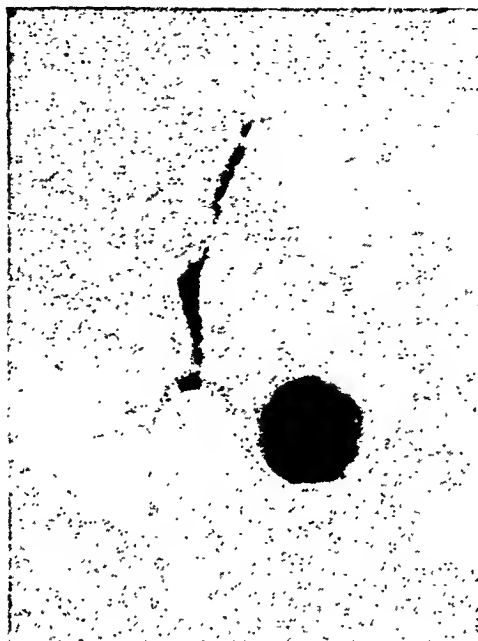


FIG. 2.

Diabetic and hypertensive retinopathy.  $\times 600$ . Haemat. + Sudan IV.  
Fatty aneurysm in connection with fatty capillary.



FIG. 3.

Diabetic + hypertensive retinopathy. Haemat. + Sudan IV.  $+150$ . Note  
the blood-filled vessel *a* with two fatty tributaries, (There are many others  
of the same type).

It is interesting to find that in some cases of hypertension a certain type of vessel exclusively is fatty (Fig. 3), neither the smaller of capillary size nor the bigger ones. I feel that the significance of this appearance needs explanation, which I have not found so far.

We recognise the fatty droplets in senile and degenerative ganglion cells (Loewenstein and MacGregor, 1943). The fat infiltration of the retinal ganglion cells in relatively young people (after thirty) is surprising and corresponds to similar changes in the brain substance. We are able to judge shape and position of fatty exudates and to decide definitely that the star-shaped exudate in the macular area is found in Henle's fibre layer.

If the specimen needs cutting we might decide to cut it with the fat reaction preserved, and we embed it, therefore, in gelatine, and section it with the freezing microtome, which makes serial investigation difficult.

No additional staining is necessary. Nuclear and fat staining show well in the section, or we embed in paraffin and section it serially, in which case, of course, there is no fat staining.

The technique of bulk investigation of choroidal tissue is similar. The hexagonal cells are so densely pigmented that they hinder the examination of the choriocapillaris. Depigmentation with potassium permanganate and oxalic acid must be carried out for a longer period than with sections. The retinal pigment is more resistant to oxydation than the branched chromatophores.

A very good view of the choriocapillaris is achieved by brushing off the hexagonal cells of their pigment content.

In such bulk specimens, stained with haematoxylin and eosin, I found in the lumen of the capillaries of the choriocapillaris large, prominent, endothelial cells, which might correspond to the "swell" cells I have described in the venules of the retina (Loewenstein, 1946).

Fatty sub-endothelial droplets in the vessels of the choriocapillaris are frequent. They are liable to escape routine examination. While investigating a considerable part of the choroid in bulk of hypertensive cases, I found only one or two bigger vessels with extensive fatty infiltrates, and the remaining choroid completely normal. I do not understand the significance of sclerotic changes of isolated choroidal arteries.

I found in different cases of uveitis studied in bulk and stained with haematoxylin—Sudan IV, masses of chromatophores filled with shining red droplets of different size, especially if the choroid has been placed outer layer upwards.

It seems that these branched chromatophores are reticulum cells which have phagocytosed fatty droplets. They mostly contain

besides fatty droplets, a granular light brown pigment. It seems that these reticulum cells have engulfed pigment granules produced by other pigment cells, the melanoblasts.

### Summary

Double staining with haematoxylin and Sudan IV with clearing of the tissue, is recommended for bulk specimens of retina and choroid. It offers a better chance of discovering such vascular anomalies as pathological anastomoses, aneurysms, sub-endothelial necrosis, and exudates in the retina, especially if fat plays a part.

The method allows a careful study of the choriocapillaris and sometimes shows fatty changes in isolated choroidal vessels. The branched chromatophores in the outer choroidal layers are frequently filled with fat, in cases of uveitis, and they are considered to be phagocytic reticulum cells.

The technique recommended is very simple, and does not presume histological experience. Even a busy practitioner may learn to do the work unsupported by a technician.

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## ANTERIOR FLAP SCLEROTOMY WITH BASAL IRIDENCLEISIS (A Preliminary Note)

BY

H. B. STALLARD

LONDON

RECENTLY I have tried a combined operation for glaucoma which I think possesses the merits of several of the accepted surgical procedures for this disorder. The operation consists in reflecting a conjunctival flap, fashioning a scleral flap hinged on the corneo-scleral junction, a limited cyclodialysis and the inclusion of a basal tongue of iris between the lips of the sclera leaving the sphincter pupillae intact. (See Fig. 1.) The results to date in 29 cases of chronic glaucoma and two of acute congestive glaucoma have been encouraging.

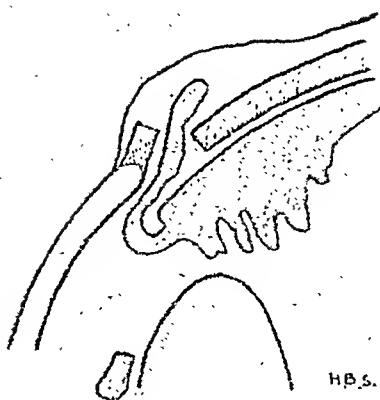


FIG. 1.

In all but one case satisfactory blebs have formed and remained, some are 6 mm. vertically and 8 mm. horizontally, and in all, the covering of conjunctiva and episcleral tissue has appeared to be substantial and in no instance thin and ectatic. (Fig. 2.) It seems on slit-lamp examination that the scleral flap is kept open on its hinges by the folded basal tongue of iris included in the lips of the

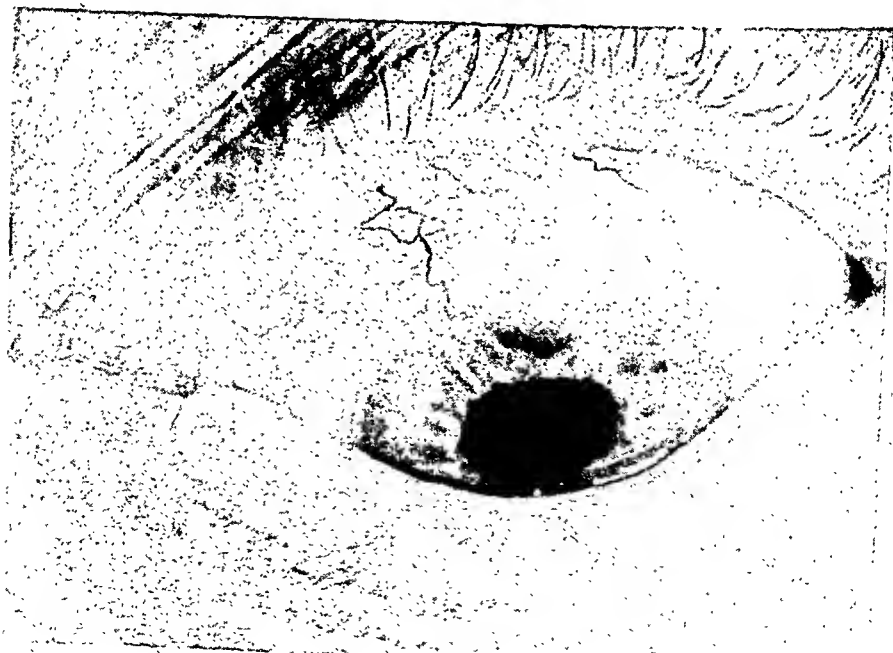


FIG. 2.

scleral incision. The intra-ocular pressure has fallen to 7-25 Hg mm. and remained so in 28 cases, and in these there has been no further field loss.

Miosis is produced before operation.

*Anaesthesia.* Pantocaine 1 per cent. and adrenalin. One ml. of novotox 3 per cent. with adrenaline 1/1,000 minims 2 is injected into the region of the ciliary ganglion and 0.5 ml. is injected into the belly of the superior rectus muscle. Pentothal and gas and oxygen may be given to nervous patients.

*Operation.* The speculum is inserted and a No. 1 white suture is passed through the tendon of the superior rectus muscle and clamped to the towel covering the frontal region. About 4 minims of novotox with adrenalin is injected beneath the conjunctiva about 3.5 mm. from the limbus from 10 to 2 o'clock so as to raise the episcleral tissues and conjunctiva.

The conjunctiva is now grasped and held forward by a pair of plane forceps 2.5 mm. anterior to the insertion of the superior rectus. The conjunctiva is snipped for about 5 mm. down to the sclera. Both blades of the spring scissors are then passed into the incision and directed temporally and downwards towards the limbus. (Fig. 3.) The blades are spread and the conjunctiva undermined. The closed blades of the spring scissors are next directed towards the nasal side and the limbus and are spread. The conjunctiva and episcleral tissues are thus undermined down to the limbus. The scissor blades are withdrawn. One blade of the scissors is then passed beneath the conjunctiva to the temporal side and slightly downwards and the conjunctiva is cut for

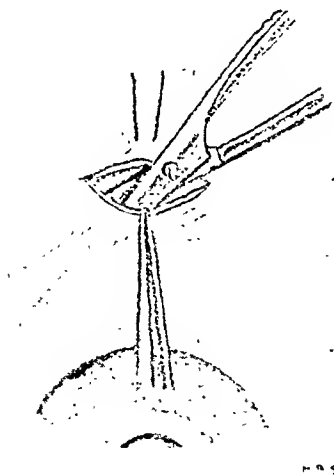


FIG. 3.

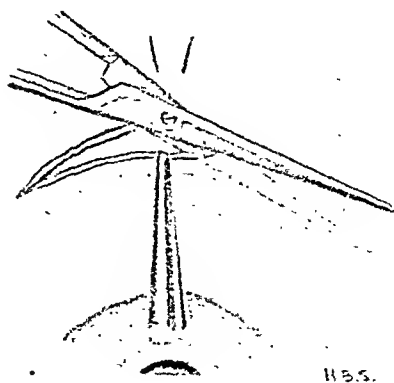


FIG. 4.

8 mm. or so from the mid-line. One blade of the spring scissors is then introduced beneath the conjunctiva on the nasal side and an incision 8 mm. or so in length is made towards the inner canthus and slightly downwards. (Fig. 4.) The conjunctival flap thus formed is turned forwards and downwards over the cornea and with a few brushing strokes from a small butter muslin swab the episcleral tissues are stripped cleanly from the sclera down to the limbus from 10 to 2 o'clock. With a double pronged conjunctival hook the conjunctival flap is held forwards and downwards by the assistant. In some cases a few strokes with Tooke's angled splitter will clear the episcleral tissue just above the limbus. Any bleeding points are checked by a touch from a heated probe. This probe also seals off any superficial episcleral vessels in the line of the scleral incision to be made 5 mm. long, 2 mm. above and concentric with the limbus.

A fine scleral hook is inserted into the sclera in the 12 o'clock meridian 2 mm. above the limbus. This steadies the eye during the scleral incision and it also retracts the anterior lip of the incision. (Fig. 5.)

The scleral incision is made with either a sclerotome or a ground-down cataract knife vertically in the sclera, that is at right angles to its surface and cleanly down to the ciliary body but not into this structure. The sclerotome has the advantage of guarded blade, the guard being set 1 mm. above the blade so that not too deep a cut is made. However, a small cataract knife used with care is very effective. When the ciliary body shows in the incision any remaining scleral fibres are divided by a few light strokes with the point of the cataract knife. (Fig. 5.) The scleral hook in the anterior lip of the scleral incision is now slightly raised and a cyclodialysis spatula is passed through the centre of the incision into the anterior end of the supra-choroidal lymph space, then on to separate the scleral spur and to enter the anterior chamber. When in the anterior chamber the spatula is moved in turn to each side of the scleral incision so as to effect a cyclodialysis 5 mm. long, that is the length of the incision. (Fig. 6.) Aqueous flows out of the incision during this procedure. The cyclodialysis spatula is withdrawn.

With the scleral hook still in place one blade of Westcott's scissors is passed on the flat into one end of the scleral incision for 2 mm. The blade is then rotated so that its cutting edge faces forwards and its blunt end is level with the corneo-scleral junction and 1 mm. nearer the mid-line than the end of the scleral incision. The blades of the scissors are closed and a converging cut is made in the sclera down to the limbus.

A similar procedure is done at the other end of the scleral incision

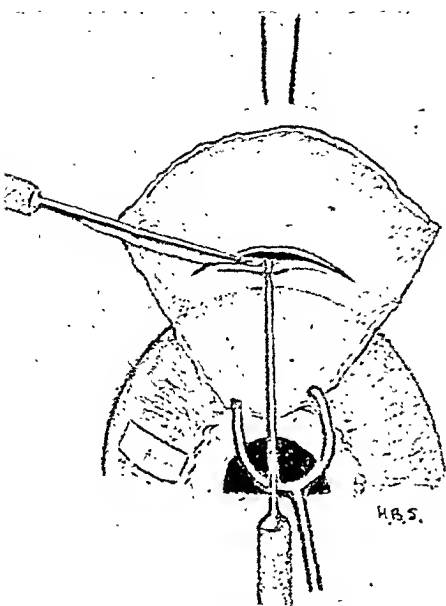


FIG. 5.

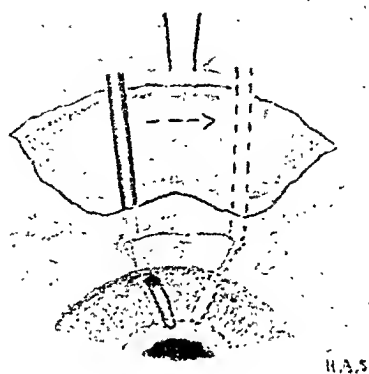


FIG. 6.

and when this is completed a hinged scleral flap is made based on the limbus. (Fig. 7.) The convergence of the lateral cuts towards the base of the scleral flap is, I am sure, important in maintaining the mobility of the flap on its hinge.

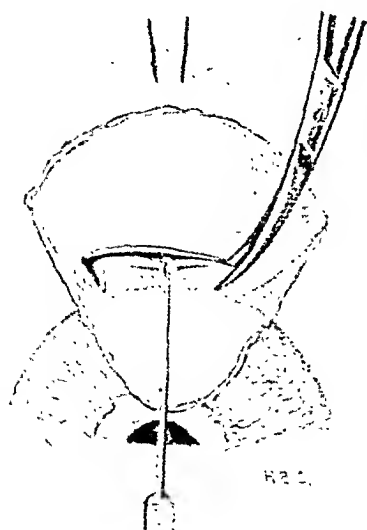


FIG. 7.

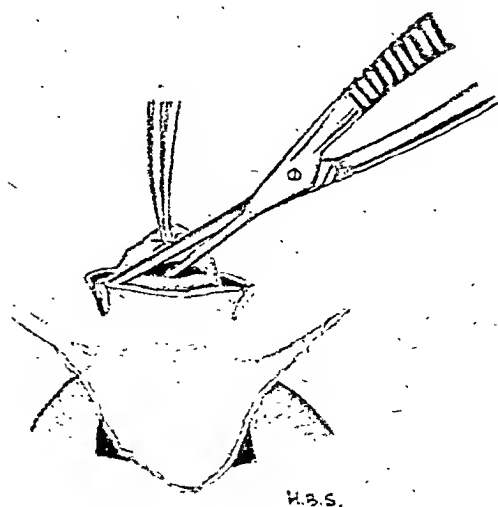


FIG. 8.



A pair of Lang's iris forceps is now introduced closed into the centre of the incision and, keeping close to the deep surface of the sclera is passed into the anterior chamber. Whilst this manoeuvre is taking place the assistant raises the conjunctival flap forwards and then upwards so that the progress of the iris forceps in the anterior chamber may be seen by the surgeon. 2.5 mm. above the pupil margin the iris forceps is opened for 2 mm. and the iris seized and drawn up into the centre of the scleral wound as the conjunctival flap is being drawn downwards by the assistant. Fine and smooth co-ordination between the surgeon and his assistant is necessary throughout this part of the operation.

A snip about 1.5 to 2 mm. long is made with fine blunt-ended spring scissors in the iris immediately in front of the forceps. One blade of the scissors is passed through the snip towards the temporal side, and a cut about 3 mm. long is made towards the iris root. (Fig. 8.) A blade of the scissors is then directed through the iris incision nasally towards its root and a cut is made for about 3 mm. The folded tongue of iris based on its root is then laid on the sclera so that about 2.0—2.5 mm. projects above the upper lip of the scleral incision.

It may be necessary in some cases to replace the pupil by passing an iris repositor into each end of the scleral incision to the side of the basal tongue of iris included in the wound and with a gentle downward stroke towards the centre of the pupil to restore its circular contour. Often it is sufficient to apply an iris repositor to the upper part of the cornea and make a downward stroke over its surface.

Penicillin is instilled on to the exposed sclera and the conjunctival flap is stroked back into place. The conjunctival incision is closed by a continuous key pattern suture of 00 black silk. A drop of atropine is instilled. Tulle gras, a pad and bandage are applied.

*Post-operative treatment and course.* There is no need for digital massage. Atropine is used at the first dressing and omitted after this. The pad and bandage are left off 48 hours after operation and the eye protected by a Cartella shield. The patient is allowed into a chair on the 4th day after operation and leaves hospital on the 8th day. The scleral flap remains open and drainage of aqueous along the tongue of iris seems to be effective as judged by the reduction of intra-ocular pressure to within normal limits and the presence of a bleb which appears 8 to 10 days after operation.

The anterior chamber is reformed on the day after operation. In one case it was lost one week after operation but reformed in 48 hours. To-date there has been no anxiety about delayed or non-reformation of the anterior chamber. A small hyphaema 1.2 mm. deep occurred in 6 cases and caused no ill effect.

Iritis occurred 3 weeks after operation in one case but there was no sign of it in any other. In this respect the post-operative course differs from that of the trephine operation where some degree of iritis commonly occurs.

To-date there has been no case of choroidal detachment and no evidence that lens opacities have appeared or increased as a result of this operation.

It has been effective in two cases of acute congestive glaucoma.

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## ALLERGIC CONDITIONS OF THE EYE\* †

### 1.—Keratitis Rosacea

BY

VERA B. WALKER

OXFORD

THE term "allergy" as used in the experimental section of this paper denotes an altered reaction rather than a hyper-sensitivity, as seen in the following example. Atropine in small doses, say one drop of 1/200 solution, dilates the pupil in 20 minutes, and in a slightly longer time causes immobilisation of the ciliary muscle and of the iris. In a few people, a much smaller dose, say 1/200,000, will produce this effect in 20 minutes, and we say they are *hypersensitive*. Occasionally we find that this smaller dose produces not only the expected reactions, but also oedema and irritation of the surrounding tissues, acute lacrymation, acute rhinitis and/or eczema of the eyelids. This is an allergic or altered reaction. In this sense one particular tissue, *e.g.*, conjunctiva, cornea or iris may be affected, and this is the usual finding; but occasionally several, and more rarely all, parts of the eye are involved simultaneously or successively.

Most allergic conditions are acute in onset and if recognised and treated at once clear up quickly, often within a few minutes or hours, leaving no permanent damage to the tissues involved. It is for this reason that this paper is entitled "Allergic Conditions of the Eye," rather than "Allergic Diseases," but it must be realised that once a tissue has remained in an abnormal physiological condition for some time, as in recurrent keratitis or iridocyclitis, there are secondary changes, due either to inflammation or to infection, which must be healed by routine treatment, though the

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\* Part of an address delivered to the British Association of Allergists at Oxford, April 17, 1948.

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allergist may be able to help in preventing a recurrence of the lesions.

We do not know why one tissue rather than another should be the "shock" tissue in any patient, and we are left wondering whether some damage, possibly congenital, and probably traumatic, must have been a forerunner of the condition. The presenting clinical signs and symptoms will depend upon the underlying structures of the various tissues involved.

In 1935 the Johns Hopkins Press published Woods' monograph on "Allergy and Immunity in Ophthalmology" in which the subject is presented from an immunologist's viewpoint, dealing with the relationship of allergy to focal infections, especially syphilis, tuberculosis and trachoma, but since that time recent work, especially in America, has shown that perhaps true allergy is rather a physiological or pharmacological abnormality, involving sensitised tissues and wet mucous membranes. In those conditions in which an infection is proved, this infection is secondary to the allergic diathesis. It will be seen from the case-sheets quoted below, that a most important point in diagnosis is an accurate family history, for almost without exception the patient has other allergic manifestations, or some of his relatives have asthma, urticaria, hay-fever or migraine.

During the last ten years many distinguished workers have written about the antigen-antibody reaction, which gives rise to the allergic reaction. Bothman<sup>1</sup> (1941) describes an allergic reaction as "an antigen-antibody reaction freeing a histamine-like substance which leads to capillary dilatation, increased permeability of vessel walls, and an exudation of serum which contains toxic substances." The earlier work was ably summarised by Duggan<sup>3</sup> (1946). He is an ophthalmologist, who, after working for some years in the Department of Physiology at the College of Physicians and Surgeons, Columbia University, stated that "To me, allergy includes all those aseptic and abacterial lesions in which the basic pathological process can be reduced to a common denominator of either increased capillary permeability or excessive contraction (spasm) of smooth muscle; or both . . . since except for the muscles of the iris and the ciliary body, most of the smooth muscle of the eye is found in the walls of the arteries and arterioles. I think that allergy of the eye can be interpreted as a problem in vascular physiology."

Whether the accumulation of histamine, due to exogenous or endogenous allergens, and the effect of that histamine on the smooth muscle of the body is a whole explanation of the changes seen, or only part of it, still remains uncertain, although Duggan's interpretation seems to offer a satisfactory explanation of most, if

TABLE I

Presenting pathology	Approximate per cent. of cases which can be proved to be allergic
Angioneurotic oedema ... ..	70
Blepharitis ... ..	10+
Conjunctivitis ... ..	40+
Keratitis ... ..	10
Keratitis rosacea ... ..	70
Iritis ... ..	3
Iridocyclitis ... ..	2.5
Glaucoma ... ..	5
Retinal haemorrhage or detachment	1
Choroiditis ... ..	3
Cataract ... ..	0.2
Migraine ... ..	54

not all, of the conditions seen in the various tissues of the eye. Depending on which tissue is sensitised to the offending allergen—i.e., the “shock” tissue—we may see angioneurotic oedema, blepharitis, conjunctivitis, keratitis, iritis, iridocyclitis, keratitis rosacea, retinal haemorrhage or detachment, choroiditis, glaucoma, cataract or migraine. From Table I it will be seen that some of these conditions are frequently allergic, and some only occasionally so. Tables II and III show that in keratitis rosacea, 70 per cent. of the cases can be satisfactorily investigated and treated by desensitisation.

### Keratitis rosacea

Rosacea, a relatively common abnormality of the skin of the face of adults between the ages of 20 and 50 years, is frequently accompanied by ocular manifestations, varying in degree from a mild conjunctivitis, through all the stages of blepharo-conjunctivitis, episcleritis and keratitis, to eventual visual incapacity. It is all too frequent to find the patient, and sometimes his doctor, too, confident that each recurrence will be less severe, and that he will “grow out of it” when aged 50. If possible before marginal vascular infiltration shows that the cornea is involved, and whether accompanied by an exacerbation of facial acne or not, a note of warning should be given. Numerous as the list of possible causes of keratitis rosacea may be, almost all authors agree that the condition is “a metabolic, rather than a local one”; digestive

upsets (Ryle and Barber,<sup>8</sup> 1920; Brown,<sup>2</sup> 1925; Eastwood,<sup>4</sup> 1928, 1934), deficiency diseases (Johnson and Eckardt,<sup>7</sup> 1940; Sydenstricker, Sebrell, Cleckley and Kruse,<sup>10</sup> 1940; Johnson,<sup>6</sup> 1941; Fish,<sup>5</sup> 1943), and hormonal disorders (Zondek, Landau and Bromberg,<sup>12</sup> 1947), all play a part, and must be treated appropriately, but even after all these have been corrected, and all bacteria removed, there is still an underlying condition which predisposes to recurrence. From a survey of the 76 cases in Tables II and III it will be seen that allergy plays a fundamental part in the syndrome:—

TABLE II

Total number of cases investigated, all with skin lesions	...	76
With conjunctivitis or blepharitis, but not yet keratitis	...	26
First attack of keratitis, 13 } Recurrences - - - 37 }	... ..	50

		Specific allergens found
Family history of allergy	... .. 56	43
Induced allergy after measles, or other high temperature disease	... .. 7	5
After "protein-shock" therapy	... .. 2	1
No explanation of allergy	... .. 11	3
	76	52=70%
Allergy not proved in	... .. 24	

## TREATMENT

*Local* (1) Removal of secondary infection with pen. ung., sulphathiazole, Dettol, or other disinfectant;

(2) Application of a dithranol\* (0.1 per cent.) cream to the skin b.d. for at least two weeks;

*General.* Desensitisation of the 52 with specific antigens by a six-weeks' course of injections;

Non-specific desensitisation of the other 24 with *Histamine-azo-globulin*, by 10 graded intramuscular injections (0.05 c.c., 0.1 c.c., 0.2 c.c., 0.3 c.c., 0.4 c.c., 0.5 c.c., 0.6 c.c., 0.7 c.c., 0.8 c.c., 1.0 c.c.) at the rate of two injections a week for 5 consecutive weeks.

If at a later date a recurrence of symptoms of either eye or face occurs, then give 0.5 c.c. histamine-azo-globulin immediately, and repeat after four days.

\* dithranol = dihydroxy-anthranol.

TABLE III

Group A = Specific allergens found (see Table II).  
 Group B = Specific allergens not found.

Year	No. of cases investigated	Recurrence in six months	Recurrence in two years
<b>A</b>			
1942	6	2	3
1943	9	1	2
1944	9	2	2
1945	10	1	3
1946	8	0	1
1947	10	2	—
	<hr/> 52	<hr/> 8	<hr/> 11/42 = 25%
<b>B</b>			
1945	2	0	1
1946	12	2	5
1947	10	3	—
	<hr/> 24	<hr/> 5	<hr/> 6/14 = 43%

$\frac{11 + 6}{42 + 14} = 39/56 = 70$  per cent. symptom-free for 2 years (both face and cornea).

The 20 cases treated in 1947 are not included in this percentage, as two years have not elapsed since completion of their treatment.

From these tables it can be seen that 70 per cent. of the patients with keratitis rosacea have not had a recurrence of symptoms within the two years following their treatment; many of these 70 per cent. are still symptom-free after three, four or five years.

There is, however, a significant difference between Group A, in which specific allergens were found, and Group B, in which all were treated with histamine. In Group A, the percentage remaining symptom-free was nearly twice as great as in Group B.

I would like to emphasise the urgency of referring all cases of keratitis rosacea to the allergists for investigation; and indeed other patients with keratitis of unknown origin, especially those with a family history of acne, eczema or urticaria, even though their own skin manifestations have not yet become obvious.

### Summary

An analysis of 76 cases of keratitis rosacea is presented. In 52 of them an allergic cause for both the skin and corneal lesions has been found.

After desensitisation, 70 per cent. of cases remained symptom-free for at least 2 years.

I take this opportunity of expressing to my colleagues at the Oxford Eye Hospital and at the Horton General Hospital, Banbury, my appreciation of their generous co-operation in this investigation; also of thanking Messrs. Parke, Davis Ltd. for supplies of histamine-azo-globulin used for 24 patients.

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## ALLERGIC CONDITIONS OF THE EYE\*†

### 2.—Migraine

BY

VERA B. WALKER

OXFORD

MIGRAINE is of importance to ophthalmologists, *first* because all humans with severe headaches, from whatever cause, eventually find their way to an eye hospital to be checked for refraction errors, and *second* because 50 per cent. of migraine cases have eye symptoms, often very severe in onset.

As early as 1820 some French authors were classifying migraine with epilepsy, eczema and asthma as manifestations of allergy, but Strümpell<sup>1</sup> (1860) was the first to suggest an allergic basis for some cases of migraine, and he spoke of it as "an exudative process comparable to urticaria and angio-neurotic oedema." Living's<sup>2</sup> (1873) monograph "On megrim" is a classical work on the subject.

In the 20th century many papers have been written quoting cases of migraine attacks in patients who gave positive skin reactions

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with certain foods or inhalants, but there has been a noticeable hesitation to claim a direct connection between the symptoms and signs. Perhaps one of the difficulties of any argument on the subject is the fact that migraine attacks usually occur in the healthiest of patients, sudden in onset, and leaving no trace of pathological abnormality when the attack is over, whether it has lasted one hour or twelve. This difficulty can be overcome if we consider allergy as a physiological, rather than a pathological response, differing from the normal in degree but not in kind.

In the 1935 Edition of Osler's<sup>3</sup> text-book, migraine is defined as "A paroxysmal affection characterized by severe headache, usually unilateral, and often associated with vomiting and/or disorders of vision." Numerous subsequent writers have elaborated this to suit individual patients or groups of patients. All cases classified as migraine in the following tables satisfy this definition.

In 100 consecutive cases of such migraine investigated in 1943-47, 54 were proved to be allergic, either by clinical trials, by skin tests, or, more often, by both methods. With each patient an attempt was made to produce a migraine attack, before prophylactic treatment was begun.

Typical examples of these patients were:—

CASE 1. Patient, male, aged 52 years. 115/75. C/o migraine + neuralgia. Duration: 8 years (about 50 attacks a year). F.H.: Asthma and migraine.

Positive allergies by skin test: Feathers + + +, Dust + + +, Cat +.

Allergies confirmed by clinical trial: feathers and dust. Treatment: desensitisation. Attacks in next 6 months, 0; attacks in next 3 years, 1.

CASE 2. Patient, female, aged 48 years. 110/80. C/o migraine. Duration: 20 years (resigned position as secretary owing to frequency of migraine). F.H.: Migraine.

Positive allergies by skin test: House dust + + +, Kapoc + +.

Allergies confirmed by clinical trial: house dust, kapoc. Treatment: desensitisation. Attacks in next 6 months, 2; attacks in next 5 years, 12.

CASE 3. Patient, male, aged 8½ years. 90/60. C/o migraine + urticaria. Duration: 4 years, in summer only. F.H.: Hay-fever and urticaria.

Positive allergies by skin test: Timothy grass + + +. Allergy confirmed by clinical trial: Timothy grass. Treatment: Desensitisation. Attacks in next summer, 0; attacks in next 3 years, 0.

CASE 4. Patient, female, aged 53 years. 121/90. C/o migraine + eczema. Duration: 25 years (irregular—usually 3 in a month). Worse in last three years. F.H.: None reported.



Positive allergies by skin test: Cheese + + +, Peas + +, Beans + +.

Allergies confirmed by clinical trial: cheese, haricot beans. Treatment: avoidance. Attacks in next 6 months, 0; attacks in next 6 years, 3.

CASE 5. Patient, female, aged 42 years. 115/80. C/o migraine. Duration: 15 years (at least once a week). F.H.: Migraine.

Positive allergies by skin test: House dust + + +, Kapoc + +.

Allergies confirmed by clinical trial: house dust. Treatment: with extracted dust from own house. Attacks in next 6 months, 0; attacks in next 5 years, 1.

CASE 6. Patient, male, aged 10 years. C/o sickness and dull headaches ("half-headaches"). Duration: 2 years. Missed 31 days at school in 1 term. F.H.: Migraine and asthma.

Positive allergies by skin test: Cat +, Dog +, Fish +, Chocolate + +, Milk + +.

Allergies confirmed by clinical trial: chocolate, cod liver oil, whole milk (unboiled). Treatment: Avoidance. Days-absent from school in next term, 2; days absent from school in next 6 terms, 3.

While these cases show that if a patient has *allergic* migraine, he can be helped tremendously by avoiding those allergens to which he is specifically sensitive, or by being desensitised; we must remember that the other 46 per cent. should be excluded from these somewhat tedious investigations, as they can derive no benefit from them. They do not belong to allergic families, and they do not present other manifestations of allergy themselves.

Realising that all patients are reluctant to give a detailed family history or an accurate personal history, other more clinical methods

TABLE I

Migraine in 100 consecutive *adult* cases

No.	Average age	Systolic pressure	Allergic origin	Per cent.
8	45	150—180	0	0
20	43	130—150	8	4
10	44	120—130	3	30
45	43	100—120	28	62
17	40	>100	15	88
100	43	—	54	—

Average for 46 non-allergic cases - - 147

Average for the 54 allergic ones - - 108

for separating the 54 per cent. allergic from the 46 per cent. non-allergic patients have been sought, and during routine general examinations significant differences of systolic blood pressures in the two groups were observed; there was no marked difference in pulse pressures.

These were all adult cases, and the pressures were all taken *between*, rather than *during* attacks. Bray<sup>1</sup> (1937) stated that in children he had not found any marked changes in the blood pressure during allergic attacks. Witts<sup>5</sup> (1933) determined the blood pressure in 440 cases of asthma, and found that the majority showed normal figures, but he did not separate the allergic asthmas from those due to other causes. From Table I it becomes clear that although *all* migraine cases do not have low systolic pressures, and all migraines are not of allergic origin, if a patient with true migraine has a low systolic pressure, then allergy should be suspected and treated appropriately.

In conclusion, attention is drawn to the apparent increase in the number of allergic patients in any community during the last two decades. They are presenting as asthmas, eczemas, conjunctivitis cases, migraines or urticarias to our general practitioners all over the country. Perhaps this increase is apparent only: it may be that many minor cases of *sub-clinical* allergy, have by the stress of present-day conditions, both mental and physical, become major cases, seeking the help of their medical advisers, and that the actual number remains fairly constant from generation to generation. Many patients seeking advice to-day for incapacitating migraine give a history of "mild half-headaches" in 1938, or even in 1928.

### Summary

(1) An analysis of 100 cases of migraine is given. Fifty-four of them were proved to be of allergic origin, and remained free from head pain after desensitisation, or avoidance of their allergens.

(2) The average systolic blood pressure of the fifty-four allergic cases was noticeably lower than that of the forty-six non-allergic ones.

(3) It is concluded that migraines in patients with a low systolic pressure are manifestations of allergy.

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# THE EFFECTS OF VARIOUS TYPES OF PENICILLIN INJECTED INTO THE VITREOUS\*

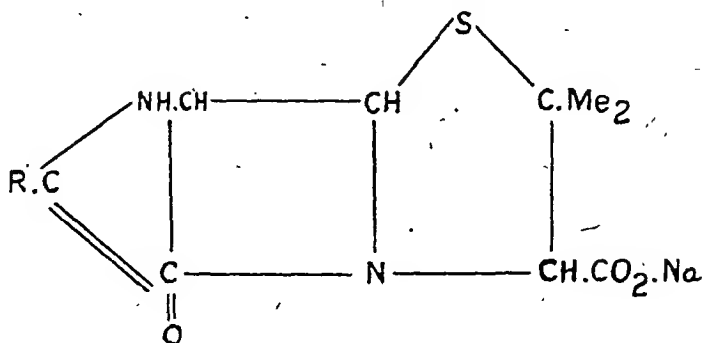
BY

P. A. GARDINER, I. C. MICHAELSON,

R. J. W. REES *and* J. M. ROBSON

FROM THE DEPARTMENTS OF PHARMACOLOGY AND PATHOLOGY, GUY'S  
HOSPITAL MEDICAL SCHOOL, AND THE TENNENT INSTITUTE  
OF OPHTHALMOLOGY, UNIVERSITY OF GLASGOW

IN a previous study (Duguid *et al.*, 1947) it was found that a solution of pure crystalline penicillin could be injected into the vitreous of rabbits, without producing any marked injury, the toxic effect being indeed much smaller than those resulting from the injection of impure preparations of the drug. Penicillin did, however, cause small areas of retinal damage in some cases. It is now known that such a pure preparation of penicillin is not a single compound but consists of at least five different compounds all similar in composition, but differing in the nature of one chemical group, viz., R, in the formula shown below:—



The different penicillins are Penicillin I (or F according to the American nomenclature), in which R is 2-pentenyl; Penicillin II (G), in which R = benzyl; Penicillin III (X), in which R = p-hydroxy-benzyl; Penicillin IV (K), in which R = n-heptyl; and dihydro-penicillin I, in which R = n-amyl. The properties of these penicillins show appreciable differences and it seemed possible that one of them might be more suitable than the others for intravitreal injection, either because it is less toxic, or diffuses away more slowly or both. Thanks to the generous supply of these substances by the Antibiotics Study Section of the U.S. Public Health Service (through Dr. Seger) we were able to undertake an

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investigation of these questions and the results are given in the present communication.

### Methods

The penicillins were dissolved in sterile saline and injected into the vitreous by the same method used previously (Duguid *et al.*, 1947). The dose introduced was 1.2 mg. or 3.0 mg. in 0.1 ml. saline. In each case the injection of penicillin was made into the vitreous of the right eye, while 0.1 ml. of saline was introduced into the vitreous of the left eye which was then used to control the clinical and histological findings in the right eye. For comparison experiments were also performed with a pure mixed penicillin (Glaxo) and the dose was 2,000 units or 5,000 units which has practically the same activity as 1.2 mg. and 3.0 mg. of penicillin II (G). The eyes, including the fundi, were always examined before the injection. The eyes were observed for periods varying from 10 to 128 days following the injections, particular attention being paid to the fundi and media. Finally the eyes were removed for histological examination. The globes were bisected in front of the ora serrata and the posterior portion examined with the help of a loupe or the slit-lamp in order to identify ophthalmoscopic changes. Portions of the posterior globe were embedded in paraffin and stained with haemalum and eosin. In view of previous findings with retinal tissue exposed to penicillin (Duguid *et al.*, 1947), and the primary intention of the experiment being to compare the different penicillins, it was not considered necessary to use further staining methods.

In the experiments on diffusion the drugs were introduced into the vitreous in the same way; 1.2 mg. in 0.1 ml. saline of penicillins G, X and K were injected into the vitreous and the animals killed after intervals of 24 and 48 hours. Samples of aqueous and vitreous were taken immediately with the eyes still *in situ*. The eyes were then removed, dissected under aseptic conditions, and samples of cornea, sclera, iris and ciliary body removed, dried on sterile blotting paper and each added to a Bijou bottle of known weight and weighed. Extraction of penicillin from the tissues by grinding in an agate mortar with sand and saline or by leaving the tissues in 0.5 ml. of saline at 4° C. overnight were tried. The latter process gave the more consistent results and was finally adopted throughout.

The penicillin estimations were made by a serial dilution method using a glucose-serum water medium with phenol red as indicator. The volume of eye fluid extract for testing was either 0.2 ml. or 0.4 ml. The Oxford staph. aureus H was the test organism and

the end point was read as the highest dilution of test fluid completely inhibiting growth of the organism, as indicated by failure to alter phenol red from red to yellow. A 1/200 dilution of an 18 hour culture of staph. aureus in glucose serum water was inoculated into each tube.

The eye fluids or saline extracts from animals not receiving penicillin were not found to have any bacteriostatic activity.

### Section 1.—The effects of the drugs on the eye

The results detailed below are based on histological and ophthalmoscopic examinations of the eyes. In some cases histological changes are present, although the clinical findings before enucleation were normal, a finding already noted by Duguid *et al.* (1947). The initial stages of the clinical changes observed ophthalmoscopically were very similar whatever the type of penicillin used. Within 48 hours of injection a certain degree of oedema was seen in some part of the inferior retina not in relation to the site of the injection which was in the upper part of the eye. A peak of oedema was rapidly reached and within 10 days it began to subside. When this oedema was very slight the retina then frequently appeared to be normal and remained so. In some cases the oedema did not disappear. Persisting fine pigment changes became visible in most of the eyes as the oedema subsided or in some cases after a latent interval.

Refractile particles similar to a localised synchysis appeared in the vitreous in a few of the rabbits injected with F, X and G. These settled on the floor of the retina after some weeks and then took on the appearance of small, hard, white particles. In most cases they were few enough to be counted, varying between 12 and about 50.

Penicillin K showed a peculiarity in that it produced new vessel formation when given in sufficient dosage.

*Mixed penicillin (pure).*—Mixed penicillin injections were given intravitreally to six animals in dosages of 2,000 and 5,000 units. The periods of observation following injection were 53 to 79 days.

Of those animals which received the smaller dose one showed retinal changes affecting the rod and cone layer over a limited area above while two showed some vacuolation of the nerve fibre layer, due possibly to oedema. Clinically no changes were noted in the retina in these cases.

Of the animals which received the larger dose, one showed an area of disturbance of the outer retinal elements. This was in keeping with the clinical appearances.

The findings in these cases are confirmatory of previous descriptions of the retina following the injection of pure mixed penicillin

(Sallmann *et al.*, 1944 ; Duguid *et al.*, 1947). It is of interest that there would appear to be no delayed effect of penicillin on the retina as the periods of observation were 53-79 days in the present series and 10-27 days in the series reported by Duguid *et al.*

*Penicillin II (G).*—Altogether 12 animals were treated with penicillin G and observed over a period of from 42-117 days. In the six eyes which received 1.2 mg. of the penicillin, no histological changes were noted other than, in one eye, the presence of a delicate non-cellular exudate lying on the surface of the retina. In two of the eyes, however, there were slight changes noted clinically. These consisted of pigmentary and atrophic changes in the anterior inferior quadrant of the fundus. It would appear that the sections do not include the affected areas in these two eyes and the histological changes can be assumed to be similar to those found in two eyes which received 3.0 mg. of the penicillin as now described. Six eyes received 3.0 mg. of the penicillin. Two showed a disturbance or loss of the outer retinal elements over a limited area. In one of these eyes there was a proliferation of pigment into the disturbed retina.

*Penicillin III (X).*—Five animals were treated with penicillin X in doses of 1.2 and 3.0 mg. and observed over a period of 50-93 days. In the two eyes which received the smaller dose no abnormality was detected in the retina. Of the three eyes which received the larger dose, two showed disturbances and loss of the outer retinal elements over fairly extensive areas with pigment migration into the retina in one of the eyes. The remaining eye of those receiving the larger dose showed non-cellular vitreous changes overlying areas of choroidal disturbance.

*Penicillin I (F).*—Seven animals were treated with penicillin F in doses of 1.2 and 3.0 mg. The periods of observation were 21 to 128 days. In the three eyes which received the smaller dose no gross retinal changes were observed but one showed changes in the internal limiting membrane of the retina which had a "blistered" appearance. Of the four eyes which received the larger dose, only one showed a normal retina. Of the others, two showed extensive areas of disturbance or loss of all the retinal elements with pigment migration while in one the changes were limited to a disturbance of the outer retinal elements.

*Dihydro penicillin F.*—Six eyes were treated with dihydro penicillin F in dosages of 1.2 or 3.0 mg. The periods of observation were 10 to 106 days. Of the three eyes which received the smaller dose, two showed areas of disturbances or loss of the outer retinal elements. Of the three eyes which received the larger dose, two showed areas with loss of the outer retinal elements, while one showed extensive destruction of all retinal elements with gross pigment infiltration of the retina.

*Penicillin IV (K).*—Five eyes were treated with penicillin K in doses of 1.2 and 3.0 mg. and observed over periods varying from 56-92 days. Of the three eyes which received the smaller dose, two showed disturbance and loss of all the retinal elements over certain areas and one of these eyes showed pigment migration into the retina. The eye which showed no retinal changes had an opacity of the lens. The two eyes which received the larger dose of penicillin K showed very extensive areas of gross destruction and atrophy of the retina with the formation of new vessels in the vitreous.

### Summary of effects of various types of penicillin on the retina

A study of these forty-one eyes shows:—

(a) All the various types of penicillin as well as mixed penicillin are capable of producing a toxic effect on the retinal cells.

(b) The changes produced are similar in kind with all the types of penicillin, excepting that only with penicillin K was new vessel formation produced. The changes consisted of localised patches of retinal destruction, the initial effect being on the outer retinal elements especially on the layer of rods and cones. In only one eye was the choroid found to be affected.

(c) The degree of change varied with the amount of penicillin introduced into the vitreous.

(d) The degree of change also varied with the type of penicillin used. In Table I the various types of penicillin are arranged in order of their increasing toxicity.

It can be seen that the toxic effects of mixed penicillin and of penicillin II (G) are the same and that both are the least toxic of the different types.

### Section 2.—The diffusion of the drugs within the eye

The diffusion of mixed penicillin when it is introduced into the vitreous has already been described (Duguid *et al.*, 1947). These authors determined the concentrations of penicillin found in the vitreous, aqueous and cornea, one hour, six hours, one day, two days, and three days after the injection of mixed sodium penicillin into the vitreous. Chemotherapeutic concentrations (*i.e.*, about 1/20 of a unit per ml.) were maintained in the vitreous for 2-3 days, and in the aqueous and cornea for 1-2 days. In the present experiments the concentration of penicillins G, X and K were tested in the vitreous, aqueous, cornea, sclera and ciliary body, 24 and 48 hours after the injection of 1.2 mg. into the vitreous and the results are shown in Table II and Fig. I. These two testing periods were

TABLE I

	No. of eyes observed clinically and histologically	No. of eyes showing no change	No. of eyes showing loss and disturbance of outer retinal elements only	No. of eyes showing loss and disturbance of all retinal elements
		All expressed as a fraction of the number of eyes examined		
Mixed penicillin (pure)	6	4/6	2/6	0/6
Penicillin II. (G)	12	8/12	4/12	0/12
Penicillin III. (X)	5	2/5	3/5	0/5
Penicillin I (F)	7	4/7	1/7	2/7
Penicillin Dihydro I (F)	6	1/6	4/6	1/6
Penicillin IV (K)	5	1/5	—	4/5

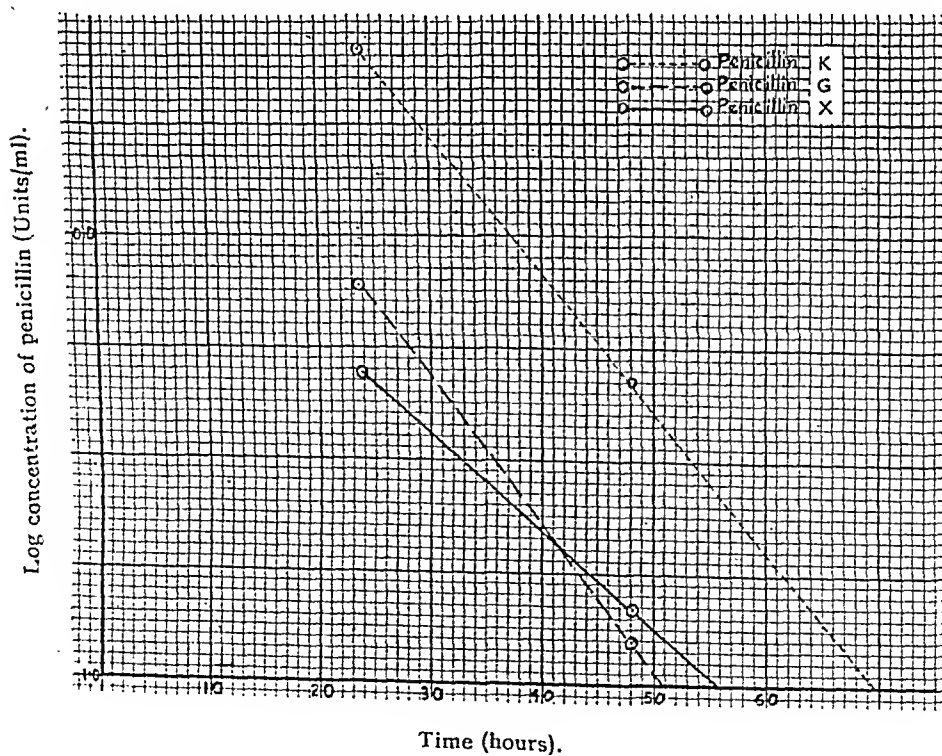


FIG. 1.

Persistence of penicillins G, K and X in the aqueous following the intra-vitreous injection of 1.2 mg. of the penicillins.



TABLE II—Concentrations of penicillins after intra-vitreous injections (1.2 mg.)

Type of penicillin	Rabbits' Number	Concentration of penicillin (U/ml.)				Concentration of penicillin (U/g.)			
		24 hours R.E.		48 hours L.E.		at 24 hours		Ciliary Body	
		Vitreous	Aqueous	Vitreous	Aqueous	Cornea	Sclera		
G	64 R.E.	80	$\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$	—	—	4.5	4.0	3.4	
	64 L.E.	80	$\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$	—	—	2.0	6.0	4.5	
	74	20	< $\frac{1}{8}$	$\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	—	3.85	2.8	
	75	20—40	1.0	1.0	< $\frac{1}{8}$	3.0	3.0	4.9	
	19	40	2.0	1.0	< $\frac{1}{8}$	2.9	5.0	6.5	
	94	40	1.0	$\frac{1}{2}$	< $\frac{1}{8}$	2.8	8.3	8.0	
X	93	80	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	1	$\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$	—	5.57	3.8	
	95	40	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	$\frac{1}{2}$ —1	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	—	3.2	5.1	
	60	80	$\frac{1}{2}$ —1.0	2.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	3.0	15.4	5.1	
	61	40	$\frac{1}{2}$ —1.0	1—2	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	5.5	8.1	4.6	
	97	20—40	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	1.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	1.5	5.0	4.4	
	98	40—80	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	2.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	2.2	5.3	7.0	
K	72	20	1.0	2.0	$\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$	—	2.1	5.7	
	113	10	1.0	2.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	—	—	—	
	144	10	$\frac{1}{2}$ —1	$\frac{1}{2}$ —1	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	2.3	—	—	
	145	40	1.0	2.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	2.8	1.2	3.0—6.0	
	152	160	> 4	2.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	3.9	> 10.6	—	
	153	10—20	1.0	1.0	< $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$	5.8	3.7	—	

considered sufficient for the purpose of determining whether there was any difference in the diffusion rates of different types of penicillin. It can be seen that there is no material difference in these rates of diffusion, although penicillin K diffuses rather more slowly. This is interesting since penicillin K is less stable than penicillin G and X when given systemically, (Coghill *et al.*, 1946.)

### Discussion

There would appear to be little doubt that penicillin K and F are the most toxic, and that mixed penicillin and penicillin G are the least toxic on the retina. In view of this it is unexpected that the toxic effects of mixed penicillin and penicillin G are the same in the eyes examined. If the eight eyes examined histologically following the injection of mixed penicillin, as reported by Duguid *et al.* (1947), are added to the present series, a comparison between the effects of mixed penicillin and penicillin G is as follows:—

	Number of eyes examined histologically	Number of eyes showing retinal degeneration
Mixed penicillin ...	14	5
Penicillin G ....	12	4

In view of these results it is probable that the mixed penicillin used in these experiments contained only small amounts of penicillins X, F and K. Unless it can be certain that a pure mixed penicillin does essentially consist of penicillin G, it would be preferable to use a pure preparation of penicillin G for intra-ocular administration, and this is in fact now available.

### Summary

(1) The toxic effects of pure mixed penicillin and penicillins G, X, F, K and dihydro F on the retina when introduced into the vitreous are compared. It is found that penicillin G and mixed penicillin are the least toxic.

(2) The diffusion rates of penicillin G, X and K when introduced into the vitreous are compared. The diffusion rates are similar and found to be comparable to those of mixed penicillin.

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